

**DISSERTATION ON**  
**“COMPARISON OF RISK OF MALIGNANCY INDEX WITH**  
**HISTOPATHOLOGICAL EXAMINATION IN**  
**OVARIAN TUMOURS”**

*Dissertation submitted*  
*in partial fulfillment of the regulations*  
*for the award of the degree of*

**M.S. DEGREE - BRANCH - VI**  
**OBSTETRICS AND GYNAECOLOGY**

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**TIRUNELVELI MEDICAL COLLEGE HOSPITAL**



**THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY**  
**CHENNAI,**  
**TAMIL NADU.**

## **CERTIFICATE**

This is to certify that this dissertation “**COMPARISON OF RISK OF MALGNANCY INDEX WITH HISTOPATHOLOGICAL EXAMINATION IN OVARIAN TUMOURS**” submitted by **Dr.ANITHA C.**, appearing for M.S. Degree Branch VI Obstetrics & Gynaecology examination in April 2015 is a bonafide record of work done by her under my direct guidance and supervision in partial fulfillment of the regulations of the Tamilnadu Dr. M.G.R Medical University, Chennai. I forward this to the Tamilnadu Dr. M.G.R Medical University, Chennai, Tamilnadu, India.

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## **DECLARATION**

I solemnly declare that this dissertation entitled “**COMPARISON OF RISK OF MALIGNANCY INDEX WITH HISTOPATHOLOGICAL EXAMINATION IN OVARIAN TUMOURS**” was done by me at Tirunelveli Medical College and Hospital, Tirunelveli 2012-2014 under the guidance and supervision of, **Prof. Dr. SHEBA ROSATTE VICTOR, MD OG** This dissertation is submitted to the TamilNadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.S. Degree in Obstetrics and Gynaecology (Branch - VI).

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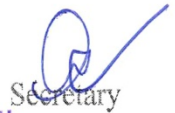
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## **ABBREVIATIONS**

USG	:	Ultrasonagraphy
RMI	:	Risk of Malignancy Index
CA 125	:	Cancer Antigen 125
PI	:	Pulsality Index
PPV	:	Positive Predictive Value
NPV	:	Negative Predictive Value
HCG	:	Human Chorionic Gonadotropin
GIT	:	Gastro Intestinal Tract
HPE	:	Histopathological Examination

# **COMPARISON OF RISK OF MALIGNANCY INDEX WITH HISTOPATHOLOGICAL EXAMINATION IN OVARIAN TUMORS**

## **INTRODUCTION :**

Ovarian cancer, the most lethal of all gynaecological malignancy represents a significant public health problem to a woman worldwide. It is often asymptomatic at an earlier stage, many of them present in an advanced stage for which the five year survival rate remains low<sup>(1)</sup>. The most important prognostic factor is the quality of primary cytoreductive surgery, and it depends on skills and experience of gynecologic oncologist. It is important to discriminate between benign and malignant tumor for selective referral of patients<sup>(2)</sup>

The current challenges associated with ovarian tumor results from a lack of effective screening strategies, difficulty in detecting the disease at an earlier stage and the disappointing impact of treatment regimens.

In Various studies it has been shown that the diagnosis of ovarian tumor by investigations like Ultrasonogram, Doppler, MRI, CT has been proved to be uncertain despite the need for expertise and they are not cost effective.

The risk of malignancy index is a simple scoring system based on combination of various clinical features. It has been developed to improve diagnostic accuracy for ovarian malignancy. This helps in selective referral of relevant patients to specialized cancer centers. Jacob et al <sup>(3)</sup> in 1990, developed a scoring system, Risk of malignancy index based on the ultrasound score, menopausal status and CA 125 value which were obtained preoperatively.

RMI at a cut off level of 200 was found to be very effective in discriminating between benign and malignant ovarian mass. Later, Tingulstad et al <sup>(4)</sup> 1996 developed RMI 2 and further it was modified by him as RMI 3<sup>(5)</sup> in 1999. Yamamoto et al in 2009<sup>(6)</sup> developed a new RMI, RMI 4 where he included tumor size score.

The purpose of this study was to evaluate the risk of malignancy index with USG score, CA-125 and menopausal status in differentiating benign and malignant ovarian masses.

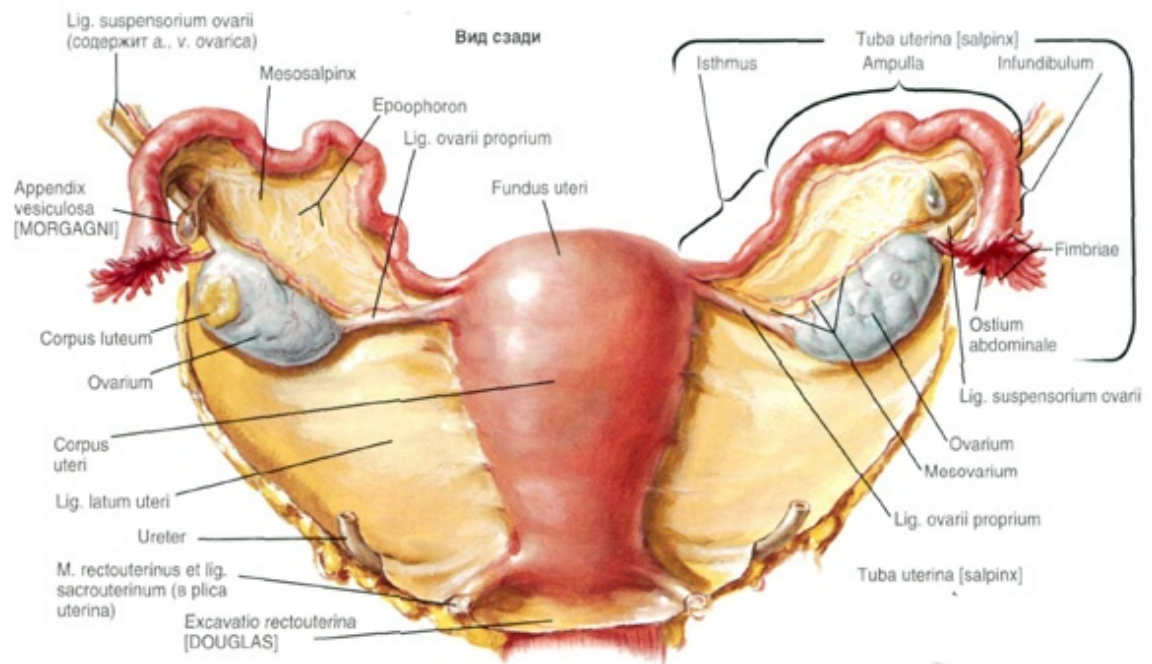
## **GROSS ANATOMY :**

### **LOCATION :**

Ovaries are paired structures located within the lesser pelvis on each side of the uterus closer to the lateral pelvic wall in the ovarian fossa at the bifurcation of common iliac artery<sup>(1)</sup> It is the only structure in the pelvic cavity which is extra peritoneal.

### **BOUNDARIES :**

Anteriorly it is bounded by obliterated umbilical ligament, by ureter and internal iliac artery posteriorly, tubal extremity attached to fimbrial end of uterine tube, peritoneal suspensory ligament of ovary which contains ovarian vessels and nerves, uterine extremity (lower pole) which is narrower than the tubal extremity is attached to lateral angle of uterus by ovarian ligament, posteroinferior to the uterine tube



Each ovary is almond shape, about 3cm long, 1.5cm wide, 1cm thick, with a volume of  $6 \text{ cm}^3$ . Before ovulation begins they are grayish pink with smooth exterior surface. After regular ovulation the surface become distorted by the scarring which follows the degeneration of successive corpus lutea.

### **BLOOD SUPPLY :**

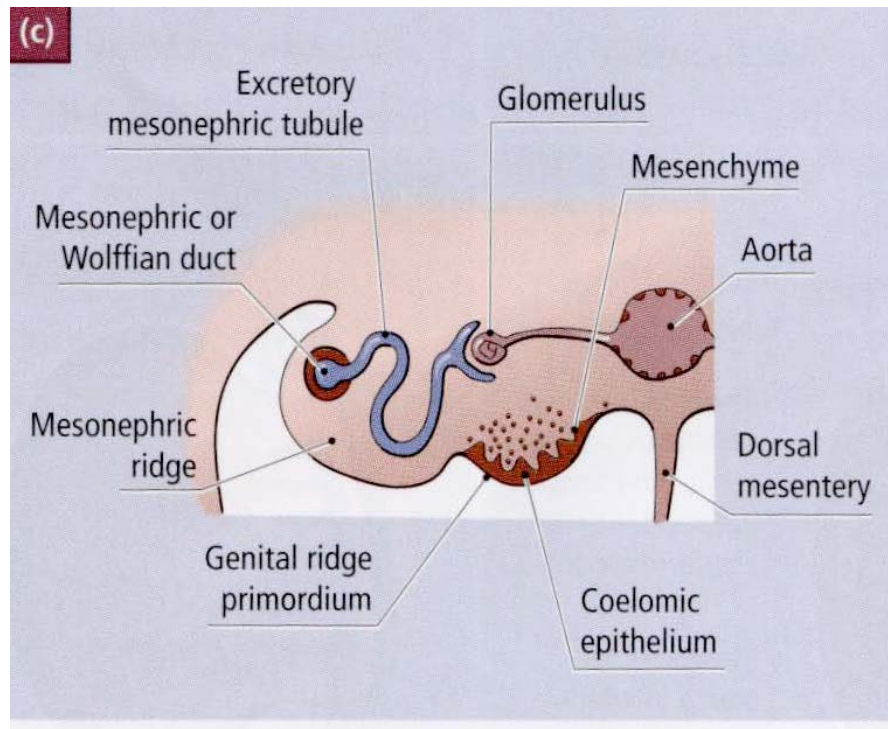
Blood supply to the ovary is through the ovarian artery both of which originate directly from the descending aorta. Both ovarian artery and vein enter and exit at the hilum of ovary through the suspensory ligament. The left ovarian vein empties into the left renal vein, and the right ovarian vein drains directly into the inferior vena cava. Nerve supply is through the ovarian, hypogastric and aortic plexus, which runs

with the vasculature through the suspensory ligament of the ovary, entering the ovary at the hilum. Lymphatic drainage of the ovary is mainly is to the lateral aortic nodes; However, the iliac nodes are also involved.

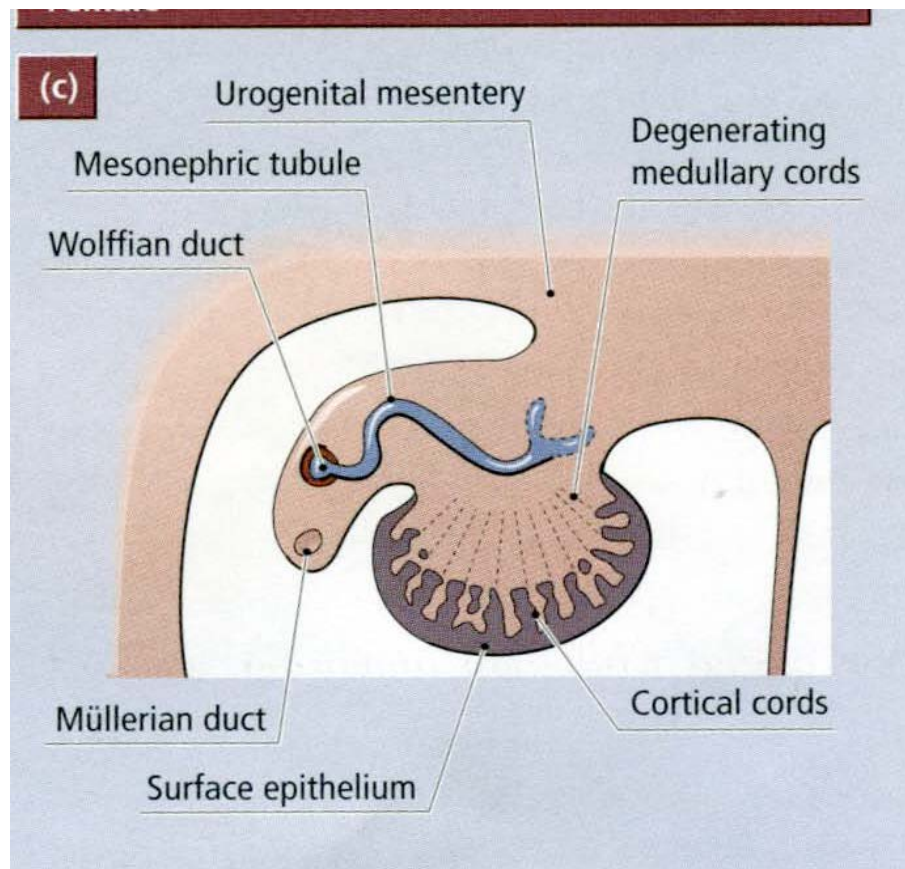
### **EMBRYOLOGY:**

On the medial side of the mesonephros Coelomic epithelium thickened to form a genital ridge. From this germinal epithelium sex cords of cells proliferate and grow into underlying mesoderm. From the yolk sac primordial germ cells migrate to the region of developing ovary and gives rise to oocytes. Each primordial germ cells are surrounded by small masses of cells which are formed by breakdown of sex cords to form primordial follicle.

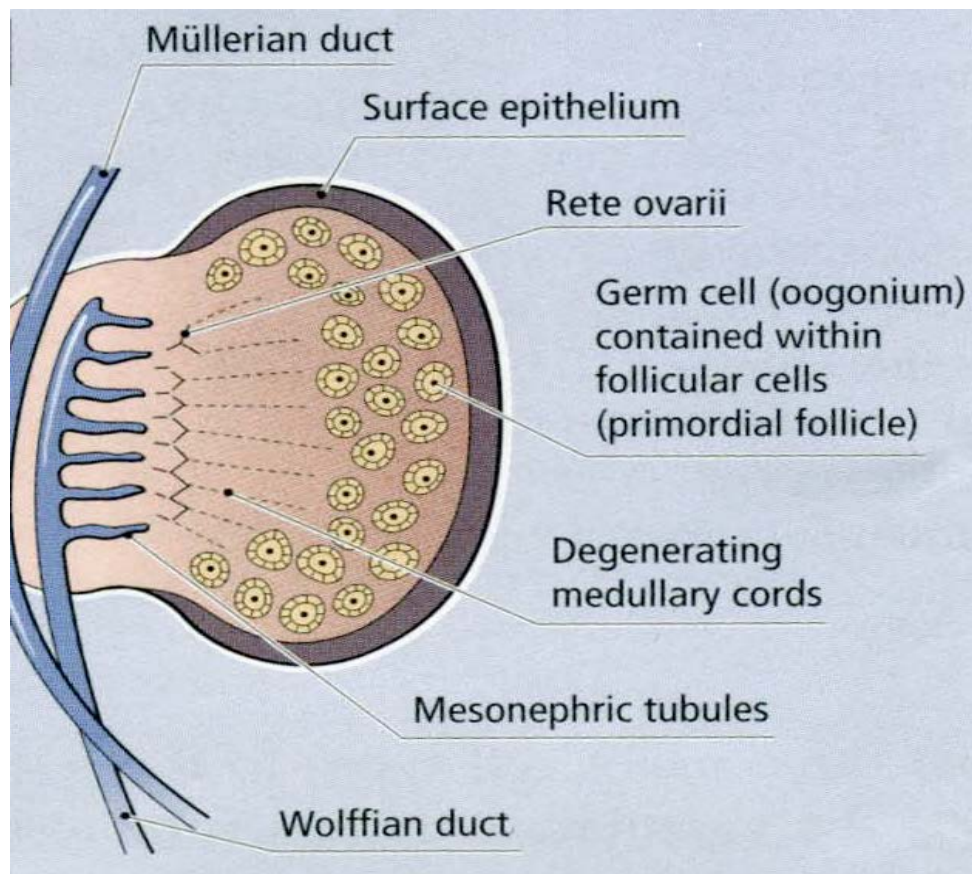
Ovaries are first found in lumbar region from where it descend down to pelvis. A gubernaculum extends from ovary to labia majora . Part of gubernaculum between ovary and uterus to form ligament of ovary, part of it between uterus and labia majora to form round ligament of ovary.



7<sup>th</sup> week



20-24WK

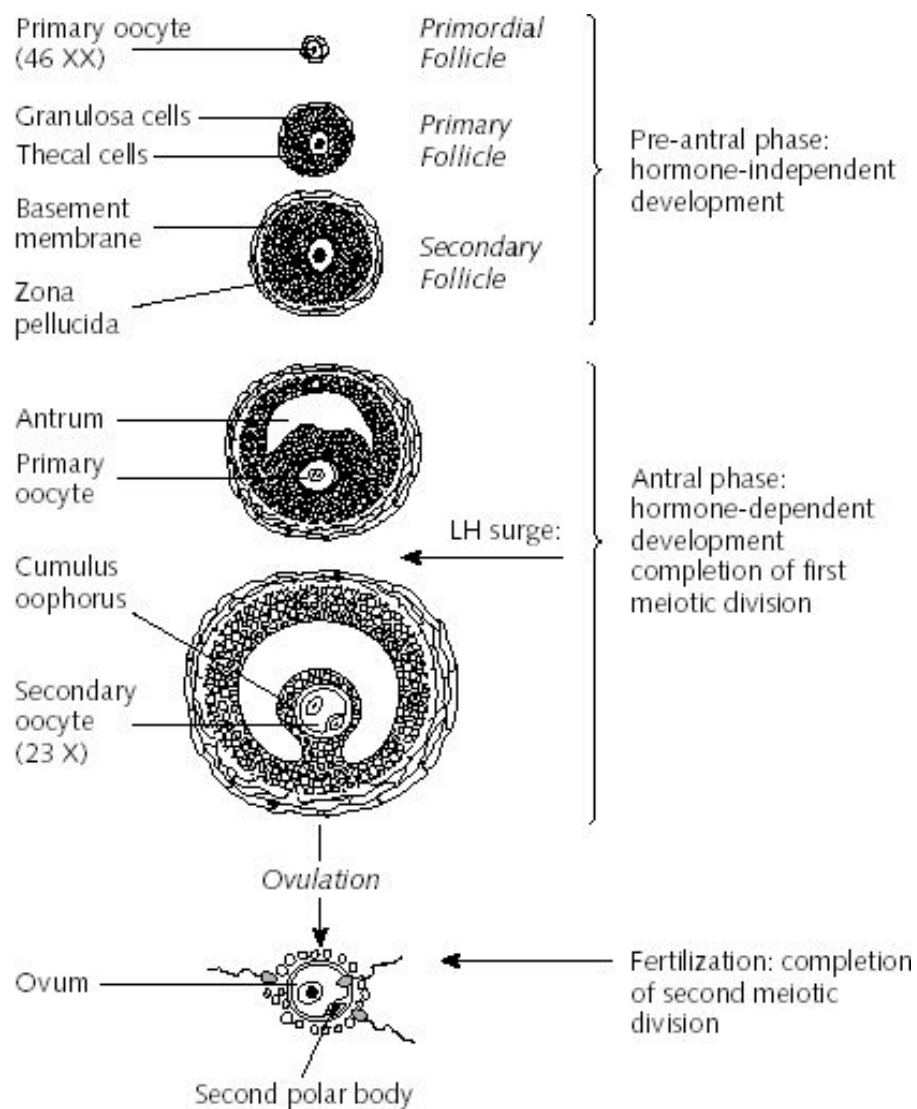




## HISTOLOGY:

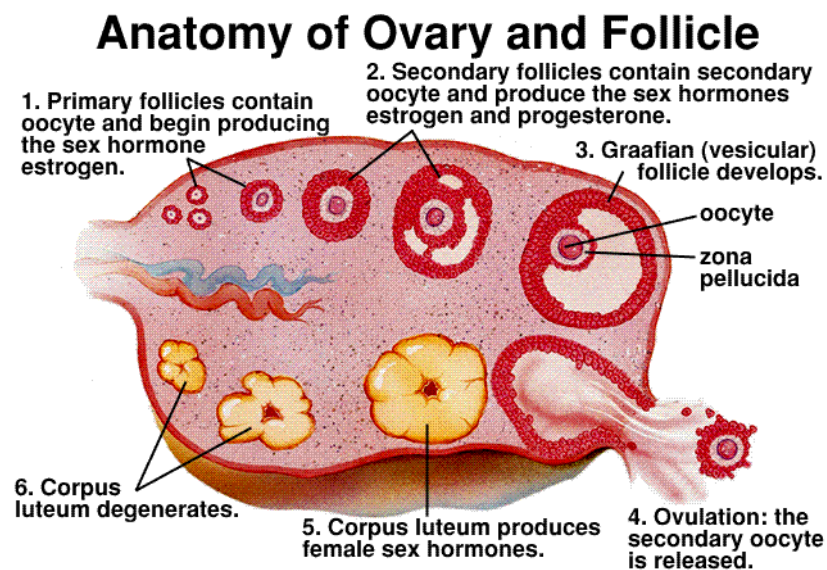
Ovary has cortex and medulla. Cortex contains follicles in various stages of development. Medulla is made of dense connective tissue which contains vessels, nerves and lymphatics.

## STAGES OF FOLLICULAR MATURATION

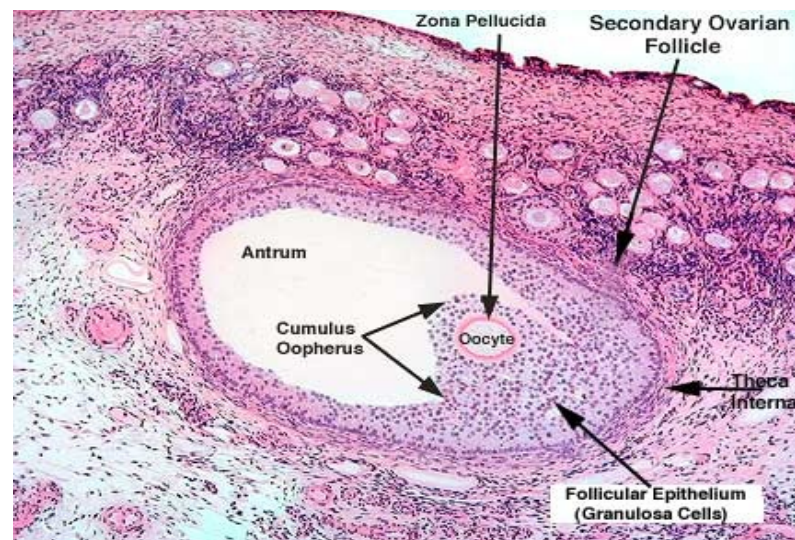
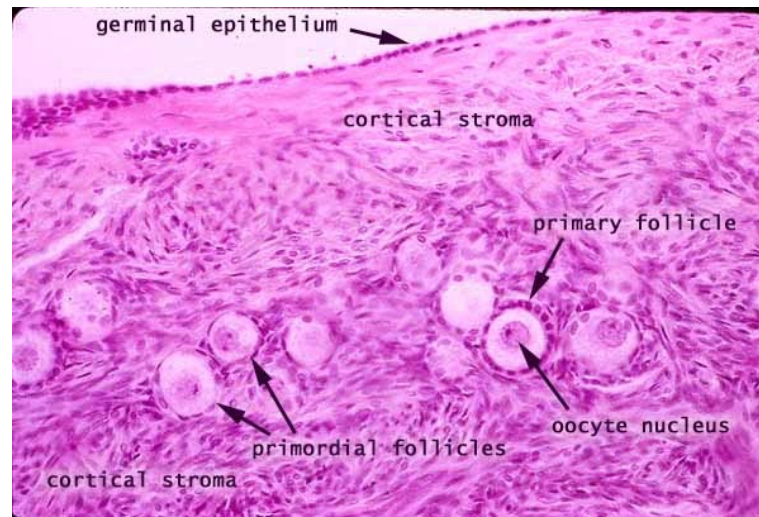


Primordial follicle is an oocyte surrounded by single layer of follicular cells, the squamous epithelium, resting in prophase stage.

In primary follicle squamous cells enlarge and become cuboidal to form granulosa cells which later on give rise to corona radiata. Proteoglycan rich zona pellucida is secreted by oocyte between its surface and surrounding granulosa cells. Primary follicle contains theca externa, theca interna, zona pellucida with gap junctions. Mass of follicular cells increase in size to form secondary follicle. Fluid filled cavities begin to form between them containing clear fluid. These cavities fuse to form one large fluid filled space surrounded by thin granulosa cells, thickened at one pole to form cumulus oophoricus.



## HISTOLOGICAL PICTURE OF FOLLICLES



## **AIM OF THE STUDY**

To evaluate the risk of malignancy index based on CA125, menopausal status and ultrasound score in women with ovarian mass, to arrive at an optimal cut off point of RMI score.

To evaluate the performance of individual parameters and RMI in differentiating benign and malignant ovarian tumors.

To validate the efficiency of risk of malignancy index in discriminating benign and malignant ovarian tumors.

## REVIEW OF LITERATURE

Ovary being a complex organ involved by variety of neoplasms accounts for 10-15% of all gynaecological cancer in developing countries<sup>(4)</sup>. Of female genital tract malignancy, ovary is the third most common site in Indian women and they account for 6% of all cancer in female. Tumors primarily from the ovary constitute 80% while 20% of the tumors are from colon, breast, stomach and uterus. The incidence as well as the survival has been increased for the past 2 decades.

Incidence of ovarian tumor increases with age, peak at about 60yrs of age. Around 80% of the ovarian cancer are epithelial adenocarcinoma of which two-third of them will be in advanced stage at the time of diagnosis<sup>(4)</sup>. Only 3% of ovarian cancer are seen in women younger than 35yrs and majority of them are germ cell tumors<sup>(3)</sup>. In premenopausal women only about 7% of ovarian epithelial tumors are frankly malignant, whereas in postmenopausal women about 30% are malignant<sup>(5)</sup>. A women's risk at birth of having ovarian cancer in her life time is around 1%-1.5% and that of dying from ovarian cancer is almost 0.5%.

## **RISK FACTORS:**

Main risk factors for epithelial ovarian cancer are

- Reproductive history
- Genetic susceptibility

### **‘NUMBER OF OVULATORY CYCLES IN A LIFE TIME BEING THE MAJOR RISK FACTOR’**

Nulliparous women were at 1.5 times the risk of parous women (Donn & Cuttler 1955). Risk decreases with increase in number of full term pregnancies. In a recent US case control study 563 cases, and 523 controls it was found that there as a reduction in risk of 40% with one child, 60% with 2 children, 80% with five or more children (TITUS; ERNSTOFF ET AL 2001). Cohort study conducted in Norway yielding 445 cases found 0.9RR for parity 1, 0.6 RR for parity 2, 0.5 RR for parity 3 or 4 in comparison to nulliparous women 10. (Kvace et al 1988).

Menstrual factors are less important than parity in an ovarian cancer risk. Menarche at an earlier age (<12) are at about 25% greater risk than those with late menarche (>15yr)<sup>(11)</sup> RISCH 1998. Women with irregular cycle length, early menopause are protective.

## **EXOGENOUS HORMONES :**

Combined oral contraceptive pills has a protective effect for ovarian cancer which has been proved beyond doubt (IARC 1999)<sup>12</sup>. Risk of ovarian cancer reduced by about 50% with 5 year use and protection increases with duration of use. (HANKINSON ET AL 1992)<sup>13</sup> (WHITEMORE ET AL). After cessation of use the effect last for around 15 years (BERAL ET AL 1999)<sup>14</sup>. Hormone replacement therapy has minimal effect on ovarian cancer (WHITEMORE ET AL 1992)<sup>15</sup> while in some have reported a moderate increase in risk (IARC1999).

## **GENETIC SUSCEPTIBILITY:**

Ovarian cancer tends to aggravate in families and such cancers tend to occur in younger age. Inheritance has a significant role in about 5% epithelial ovarian cancer, and they are usually serous adenocarcinoma. BRCA1, BRCA2 Mutations are implicated in 5-10% of malignant ovarian tumours., They also have an increased risk for lynch syndrome (colon, endometrium, ovarian cancer)<sup>16</sup>. Women with an inherited BRCA1 gene has 66% risk of breast cancer and 40-50% risk of ovarian cancer .With BRCA2 penetrance of breast cancer is 80% but for ovarian cancer penetrance is only 25% .With one affected family member, relative risk of ovarian cancer was found to be 3,and with 2 relative risk was found to be 7. Prophylactic Oophorectomy considered in

BRCA1 Mutation carrier as they have a lifetime risk of around 36% (Risch et al 2001) of developing ovarian cancer.

### **OTHER FACTORS:**

#### **DIETARY FACTORS:**

Case control studies in both China<sup>(20)</sup> & Italy<sup>(21)</sup> found that high intake of fat and meat are associated with ovarian cancer. In Italian study, it was found that red meat increase the risk by 50% while vegetables decreases it by 50%.

Use of talc powder in genital hygiene associated with 1.5 relative risk of ovarian Cancer.

### **CLINICAL FEATURES:**

Majority of women with ovarian mass are asymptomatic in an earlier stage, they often present with vague and nonspecific symptoms. In pre and postmenopausal women, the presence of vague symptoms like dyspepsia, early satiety, loss of appetite, urinary frequency and / or urgency, altered bowel habits for more than 12 days per month should alert the treating physician. In the reproductive age group ovarian masses are mostly functional and can be managed conservatively or with minimal invasive procedures. The Probability of malignancy is high in pre and postmenopausal women and they should be properly investigated and



evaluated. Careful physical examination, imaging techniques will be helpful in arriving at a diagnosis. The Ultrasonogram is the preliminary imaging technique in patients with pelvic adnexal masses. Used in screening (endometrium, ovary), diagnosis (evaluation of the adnexal mass) and follow-up of therapy for detection of recurrences. Ovarian cancers are detected in late stages due to lack of symptoms so the 5-year survival rate of women with epithelial ovarian cancers has not changed much over the years despite the advances in surgery and chemotherapy. Ultrasound is used as a screening tool for ovarian malignancy based on its ability to detect tumors which are asymptomatic and not clinically palpable. In the early days, ultrasound was used alone and was not considered as a useful tool for screening.

The feature that are suggestive of malignancy in an ultrasonogram are

1. Bilateral lesion
2. Multiloculated lesion
3. Ovarian volume more than 10cm<sup>3</sup>
4. Cyst wall thickness more than 3mm
5. Septal thickness more than 2mm
6. Solid component / complex mass (Solid & Cystic)
7. Papillary excrescences
8. Increase in vascularity

9. Doppler resistance index less than 0.40 ( $RI < 0.40$ )

10. Presence of ascites

11. Presence of intrabdominal metastasis

The sensitivity of USG is high but the specificity is low for diagnosis of early ovarian malignancy. Granberg et al in 1993<sup>(24)</sup>, reported that ultrasound reliably predicts ovarian cyst characteristics. The percentage of malignancy was 0.3% in unilocular cyst, 7% in unilocular cyst with solid component, 36% multilocular lesion and 39% in solid tumor.

Sassone et al<sup>(25)</sup> in 1991 developed index based on 4 different ultrasonographic features like structure of internal wall, thickness of the wall, the presence of septations and echogenicity. It has 100% sensitive and 83% specific in differentiating benign from malignant ovarian masses.

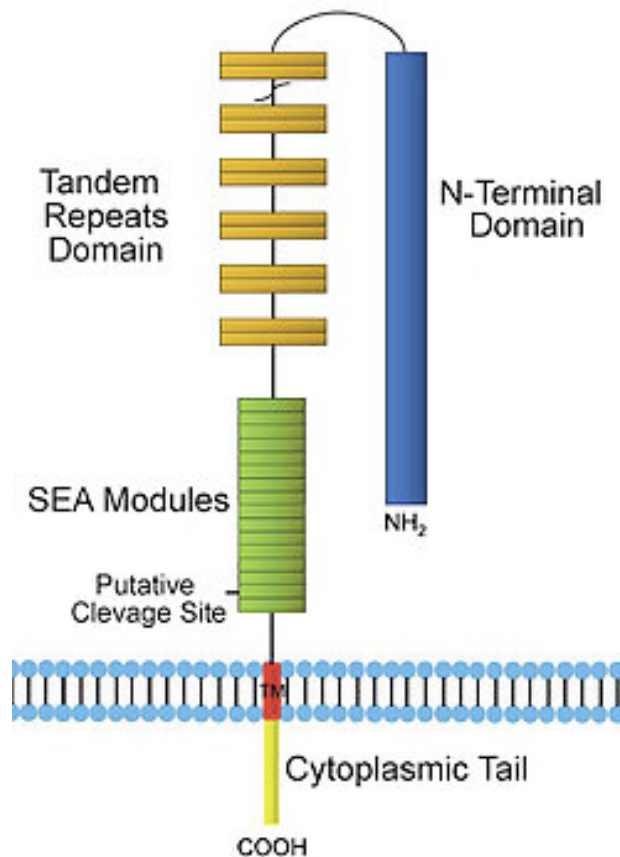
In 1993 De Priest et al<sup>(26)</sup> reported a index system based on 3 structural characteristics, combined tumor volume, wall structure and septal structure. This was tested on 213 ovarian masses, sensitivity and specificity was found to be 89% and 70% respectively.

Botta and Zarcone in 1995 compared the diagnostic accuracy of the Sassone<sup>[25]</sup> and De priest<sup>[26]</sup> scoring systems. It was found that cut of

value of 5 in De priest scoring system and cut off value of 9 in Sassone<sup>[25]</sup> scoring system has a large number of false positive results. There was considerable overlapping of scores between benign and malignant tumors. They concluded that the addition of ovarian volume as a criteria did not improve the accuracy of scoring system. In 1997, Ferrazzi et al<sup>[27]</sup> produced a morphological scoring system tested on 330 ovarian tumors, a new multicenter score demonstrated a statistically significant diagnostic accuracy. This was due to addition of two new criteria that allowed correction for typical dermoids and 10 endohaemorrhagic corporalutea. This index has a sensitivity of 87% and specificity of 67%. This study gave better result than other previous scoring system (Sassone et al 1991<sup>[25]</sup>, Granberg et al<sup>[24]</sup> 1993 etc) in predicting the malignancy. However, none of these scoring systems have very high accuracy.

### **CA 125:**

CA 125 is the serum based tumor marker used in screening of ovarian tumor first described by Bast and colleagues in 1983. It is also known as tumor associated protein because elevated levels does not always indicate ovarian malignancy, that is its levels can be high even without malignancy or disease.



### CA 125 TEST:

CA 125- cancer Antigen 125 (tumor cell surface signal) was so named because it was the 125<sup>th</sup> antibody tested against ovarian cancer cell. CA 125, a level of 35U was found to be the cut off, as 99% of healthy women will have values less than 35, while women with ovarian cancer will have values in hundreds even in thousands. CA 125 is not specific for ovarian cancer especially in reproductive age, where the various benign conditions associated with elevated CA 125 levels are more common. Hence in post menopausal women the cut off value of CA

125 in predicting malignancy is 35U/ml whereas the cut off value upto 200 U/ml is not very predictive in premenopausal women.

Only 50-60% of women with early stage, and 80-90% of women. With advanced stage ovarian cancer will have elevated values. Due to its low sensitivity and specificity, CA 125 values are not useful in screening the general population. However high risk women should be subjected to CA-125 test.

#### **CA-125 & FALSE ELEVATION:**

Low levels of CA125 are persistently released by normal tissues including ovarian cells, pancreatic cells, breast cells, and tissue lining the abdomen and chest. Ovarian cancer not only increases the number of cells that secrete CA125 but also inflames the lining of abdomen which contains normal cells that release CA125. So not only the ovarian cancer but also some other cancer in the abdomen elevates CA125 levels. Non cancerous condition which elevates the levels are inflammatory condition of the abdomen, (Diverticulitis, Peritonitis, Inflammatory bowel disease, Pelvic inflammatory bowel disease, tuberculosis, pancreatitis).

Liver diseases, recent surgery, benign gynaecological conditions such as fibroid, endometriosis, ectopic pregnancy and ruptured cyst, pregnancy, lung and colon cancer.

#### **FOUR MAJOR ROLE OF CA 125 :**

1. Predicts treatment outcome in women with ovarian cancer, fallopian tube cancer and primary peritoneal cancer.
2. Helps in detection of recurrent ovarian cancer.
3. To monitor and assess the treatment effectiveness throughout the course of Chemotherapy.
4. Used in screening of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer in high risk cases .CA 125 test can be helpful but it is hard to interpret so serial measurement over a course of time may be helpful rather than a single value.

Various other tumor markers used for screening ovarian cancer are HE4, CA 19-9, CA 15-3, lipid associated sialic acid, osteopontin etc. Proteomic analysis in serum of women with elevated CA125 which detects the proteins & protein fragments in the circulating blood helps in differentiation of benign and malignant ovarian tumors. The sensitivity, specificity and the positive predictive value of proteomic pattern are 100%, 95% & 94% respectively. But its efficacy is yet to be studied in large population. In women with family history of epithelial ovarian cancer genetic testing is advocated.

None of the investigational modalities are proved to be efficient in differentiating benign and malignant ovarian tumors. To improve the sensitivity and specificity of the test in predicting the presence of malignancy a multimodal screening modalities was introduced, which combines various parameters Jacob et al<sup>(3)</sup> in 1990 introduced a new scoring system called Risk of Malignancy index (RMI).

RMI is based on the following 3 parameters.

1. Serum CA 125 level (U/ml).
2. Ultrasound score.
3. Menopausal status.

Ultrasound findings such as bilateral lesions, multilocular cyst, presence of solid lesion, presence of metastasis, ascites. Each scored one point. If none of them are present ultrasound score is 0, if 1 of the finding is present then the score is 1 and if 2 or more finding are seen then the score will be 3.

1) The menopausal status (M), In premenopausal M=1 and In Postmenopausal M=3 RMI is the multiplied factor of CA 125, Ultrasound score, and Menopausal status. It is expressed as,

$$RMI = U \times M \times CA\ 125$$

The sensitivity and specificity Of RMI with Cut off level of 200 was found to be 71% and 96% respectively, positive predictive value of 89% for diagnosing ovarian cancer.

Davis et al in 1993 <sup>(28)</sup> conducted a study involving 124 patients to validate the Risk of malignancy index. This study confirmed that in differentiating benign and malignant Risk of malignancy index is more efficient than the individual criteria and the results were compared with the other scoring systems. In this study, the sensitivity and specificity of RMI was found to be 87% and 89% respectively. Hence concluded that RMI is a simple scoring system that will be helpful in differentiating benign from malignant ovarian lesion and provides an opportunity to refer appropriate cases to tertiary care centre, where surgery can be done by gynaec oncologist.

In 1996 Tingulstad et al modified the risk of malignancy Index RMI1 proposed by Jacob and named as RMI 2. The same parameters are used as in RMI 2 but the scoring system was altered.

1. CA 125 level (value in U/ml)
2. Menopausal score M ( Premenopausal M=1, Postmenopausal =4)
3. Ultrasound score U (based on USG features like bilateral lesion, multiloculation, solid lesion, ascites and metastasis).



Each parameters were given 1 point. If the points were 0 or 1  $U=1$ , and if two or more parameters were present  $U=4$ . The sensitivity and specificity of RMI 2 was found to be 80% and 92% respectively and the positive predictive value of 83%. Comparison of RMI2 with RMI 1 revealed that RMI 2 was efficient in predicting malignancy.

Leelahakorn et al in 2005<sup>(29)</sup> studied the role of CA125, Menopausal status, and ultrasonographic score in discriminating benign and malignant ovarian tumors. In this study he had a sensitivity of 88.6%, specificity of 90.7%, positive predictive value of 70.5%, and negative predictive value 97% respectively.

Tingulstad et al (5) in 1999 further modified RMI 2 which was previously modified from RMI 1 by altering the scoring values and it is now termed as RMI 3.

The scoring of RMI 3 is different from RMI 1 and RMI 2.

1. CA 125 value is the absolute value.
2. Menopausal score in premenopausal  $M=1$  and in Postmenopausal  $M=3$ (similar to RMI1).
3. The ultrasound score  $U$  is based on presence of like bilateral lesion, multiloculations, presence of solid areas, ascites and metastasis.

Ultrasound Score 0 or 1 made U=1

Score 2 or more made U=3

The study involving 365 patients with a cut off value of 200, the sensitivity, specificity, positive predictive value and negative predictive value of RMI 3 was found to be 71.1%, 92%, 69% and 92% respectively.

In Conclusion, it was found that RMI 3 has high sensitivity and specificity in diagnosing ovarian cancer. RMI scoring system is more efficient than individual parameter in discriminating ovarian tumor as benign or malignant.

Morgante et al 1999(30), Leelahakorn et al 2005(29), in a study reported that with an ultrasonographic techniques alone sensitivity and specificity in diagnosing malignant ovarian cancer are 62% and 73% respectively. Benjapibal et al 2007<sup>(1)</sup>, elevation of CA 125 is noted in 85% of surface epithelial ovarian tumors. With a cut off of 35U/ml the sensitivity and specificity was 83% and 39.3% respectively. Yamamoto et al in 2009, further modified the risk of malignancy index by introducing tumor size score.

RMI 4 is the multiplied factor of CA 125 level, ultrasound score, and menopausal status and tumor size score.

$$\text{RMI 4} = \text{CA 125} \times \text{U} \times \text{M} \times \text{S. (CUT OFF VALUE} \rightarrow 450 \text{)}$$

- CA 125 level – the absolute value in U/ml
- Menopausal score In Premenopausal M=1 and in  
Postmenopausal M=4
- U ,ultrasound score based on
  - \* Bilateral lesion
  - \* Multilocularity
  - \* Solid areas,
  - \* Ascites and
  - \* Metastasis

U= 0 Or 1 made U=1

U=2 or more made U=4

- S→ tumor size score.

S =1, if tumor size is < 7 cm in a single largest diameter and

S =2 if tumor size is 7cm or more.

The study showed that Inclusion of tumor size score in RMI 4 improved the efficiency to diagnose malignancy. Comparing with other three indices RMI 4 has better sensitivity and specificity in differentiating malignant and benign ovarian tumors. This study has a sensitivity of

86.8%, specificity of 91%, positive predictive value of 97.5% and negative predictive value of 90%. It was concluded that RMI 4 was better than RMI 1, 2 & 3.

## RISK OF MALIGNANCY INDEX

S.NO	PARAMETERS	RMI 1	RMI 2	RMI3	RMI 4
1	CA 125	U/ml	U/ml	U/ml	U/ml
2	Ultrasonogram score				
	If U=0	U = 0	U=1	U = 1	U = 1
	If U=1	U = 1	U=1	U = 1	U = 1
	If U=2 or more	U = 3	U=4	U = 3	U = 4
3	Menopausal Status				
	-Premenopausal	1	1	1	1
	- Postmenopausal	3	4	3	4
4	Tumor size score				
	size <7cm				S = 1
	size >7cm				S = 2

Manjunath et al in<sup>(31)</sup> 2001 reported a study , comparing the Risk of Malignancy indices RMI 1, 2 and RMI 3 in discriminating benign and malignant ovarian tumor. It was found there was no statistical difference in all three RMI indices in differentiating benign and malignant ovarian tumors.

In 1999 Twickler et al<sup>(32)</sup> devised “The Ovarian Tumor index’ to predict the risk for malignancy. The study involved 244 women, of which 214 had benign lesions and 30 had malignant lesions. The ovarian tumor index is found to be accurate in predicting the ovarian malignancy by combining various parameters like age in years, ovarian volume, Sassone’s<sup>[7]</sup> morphology score, PI, central or septal location, peripheral location and echogenicity.

In 2002 Torres et al<sup>(33)</sup> devised a study on 158 patients with ovarian mass and the study showed that the sensitivity and specificity of RMI to be 73% and 86% respectively.

In 2003, Anderson et al<sup>(34)</sup> conducted a study involving 180 patients to demonstrate the ability of RMI in discriminating benign and malignant ovarian tumor. The sensitivity of RMI With cut off value of 200 sensitivity, specificity, positive predictive value, and negative predictive value was found to be 70.6%, 87.7%, 66.1% and 89.8% respectively.

Ma et al in 2003 devised a study on 140 patients and evaluated the Risk of Malignancy index in a woman with pelvic mass preoperatively. The sensitivity, specificity, positive predictive value and negative predictive value was found to be 87.3%, 84.4%, 82.17% and 89%

respectively. In conclusion, there was no statistically significant difference between RMI 1, RMI2, and RMI3 in differentiating benign and malignant ovarian tumor and also demonstrated that RMI to be valuable and in predicting ovarian tumor preoperatively.

In 2004 Obeidat et al<sup>(35)</sup> conducted a study in 100 women with ovarian mass to validate the risk of malignancy index. The sensitivity, specificity, positive predictive value, negative predictive value was found to be 90%, 89%, 96% and 78% respectively with cut off value of RMI 200. They showed that RMI is a suitable scoring index.

Van den Akker et al<sup>(36)</sup> in 2010 reported a study involving 548 patients to evaluate the Risk of malignancy index in daily basis. With a cut off value of RMI 200, sensitivity, specificity, positive predictive value and negative predictive value was found to be 81%,85%,48% and 96% respectively. RMI is a simple scoring system that helps in diagnosis ovarian cancer during the preoperative period.

Leelahakorn et al<sup>(37)</sup> in 2005 conducted a study in 175 women with pelvic adnexal masses. With a cut off value of RMI 200, the sensitivity was 88.6%, specificity was 90.7%, positive predictive value was 70.5% and negative predictive value was 97%. The RMI which was calculated in the pre operative period was compared with histopathology report in the

post operative period. They concluded that RMI is a reliable scoring method in detection of ovarian malignancy. In this study, the Ultrasound scoring system of Ferrazzi et al 1997 <sup>(40)</sup> was used in the calculation of RMI.

In 2007 Ulusoy et al<sup>(38)</sup> evaluated 296 patients with adnexal masses with RMI. With the cutoff of 200 the sensitivity, specificity was, the positive predictive value and negative predictive value was found to be 71.7%, 80.5%, 67.3%, 83.6% respectively.

Milan Terzic et al in 2011 conducted a study involving 81 patients out of which 51 had benign tumors and 30 had malignant ovarian tumors. With a cutoff value of RMI 200, the sensitivity, specificity, positive predictive value and negative predictive value was found to be 83.33%, 94.12%, 89.29%, 90.57% respectively.

Rachmasari Putri et al in 2010 retrospectively analysed 90 patients and calculated the Risk of Malignancy index score. Out of 90 patients, 70 Of them had malignancy and 20 of them had benign tumors. With the cutoff of RMI 200 the sensitivity, specificity, positive predictive value and negative predictive value was 70%, 75%, 90.74%, 41.67% respectively. They concluded that RMI is very reliable method in diagnosing malignancy.



Monirath Hav et al in 2011 conducted a study involving 151 patients with adnexal masses. Out of them 132 patients are found to have benign mass, 19 were diagnosed to have malignant mass. The study showed that the performance of RMI was good with the cutoff value of  $RMI = 238$ . The sensitivity, specificity, the positive predictive value and negative predictive value was found to be 89.5%, 96.2%, 77.3%, 98.4% respectively.

Erfan Akturk et al in 2012 devised a study that compares the four risk malignancy indices RMI 1, RMI 2, RMI 3 and RMI 4 involving 100 patients with ovarian mass. The study concluded that there is no statistical difference between RMI 1, RMI 2 and RMI 3 at a cut off value of 200 and RMI 4 at the cut off value of 500. The sensitivity, specificity, positive predictive value, negative predictive value of RMI1, RMI 2, RMI 3, RMI 4 were obtained and there was no statistical difference between them and their diagnostic performance were same. Thus RMI is a simple scoring system and any of them can be used even in unspecialised units and is highly useful in proper selection of patients who require referral to specialized centers. Risk of malignancy index further helps in differentiation of benign disease that needs conservative line of management or minimal invasive procedures, thus avoids unnecessary surgical exploration of patient with benign diseases. The study showed

the RMI should be the test of choice in discriminating benign and malignancy conditions in the preoperative evaluation of patients.

Bouzari Z et al in 2012 reported a study in 182 patients presented with ovarian mass and evaluated the ability of RMI index in diagnosing malignant ovarian tumor. At a cut off value of 200, the sensitivity, specificity positive predictive value and negative predictive value of the RMI were 91.3%, 88%, 52% and 98.5% respectively. At a cutoff point of 265 they concluded that the sensitivity, specificity, positive predictive value and negative predictive value were high in differentiating benign and malignant ovarian tumors. The sensitivity and specificity was 91.3% and 96.2% respectively at a cut-off point of 265 which was based on the receiver operating characteristic curve.

Hakansson F et al in 2012 conducted a prospective study involving 1159 patients with pelvic masses in tertiary oncology centre. The objective of the study was to assess the ability of RMI with cut off value of 200 for preoperative diagnosis of ovarian malignancy. The sensitivity, specificity, positive predictive value and negative predictive value were 92%, 82%, 62%, 97% respectively. From the study, he concluded that Risk of malignancy index has high diagnostic performance in differentiating benign and malignant ovarian tumor which enables the patients to undergo further evaluation if needed.

In 2012 Wang et al <sup>(47)</sup> devised a study on 180 patients with ovarian tumor by applying an improved risk of malignancy index. The improved RMI is modified from Jacob et al by introducing colour doppler study and new tumor marker (Tumor specific growth factor). Improved RMI is redesigned by including ultrasound score, Tumor specific growth factor levels and colour doppler flow imaging result. Improved RMI has high sensitivity, specificity, positive predictive value and negative predictive value and therefore has a better performance in diagnosing malignant ovarian tumor than RMI. He showed that, in comparison of classic Jacob's model the improved RMI was accurate in predicting germ cell tumor, granulosa cell tumor and ovarian malignancies in early stage when compared to Jacobs RMI. But this can be applicable only in tertiary centers where high level of expertise in ultrasonogram and sophisticated Doppler are available.

Ovary being a complex organ said to be involved by wide variety of neoplasms. It is the only organ in the body which gives rise to galaxy of neoplasms.

Ovarian tumors are classified into benign and malignant groups, and the third group intermediate between the two are called borderline ovarian tumor which was introduced by WHO and FIGO in 1971.

Borderline ovarian tumor, the tumor of low malignant potential shows higher proliferative activity when compared to benign neoplasms but does not show stromal invasion. They remain confined to the ovary for longer period, and are associated with a very good prognosis, occur predominantly in premenopausal women between the ages of 30 and 50 years of age , while invasive carcinomas occur between the ages of 50 and 70 years of age.

The criteria for the diagnosis of borderline tumors are

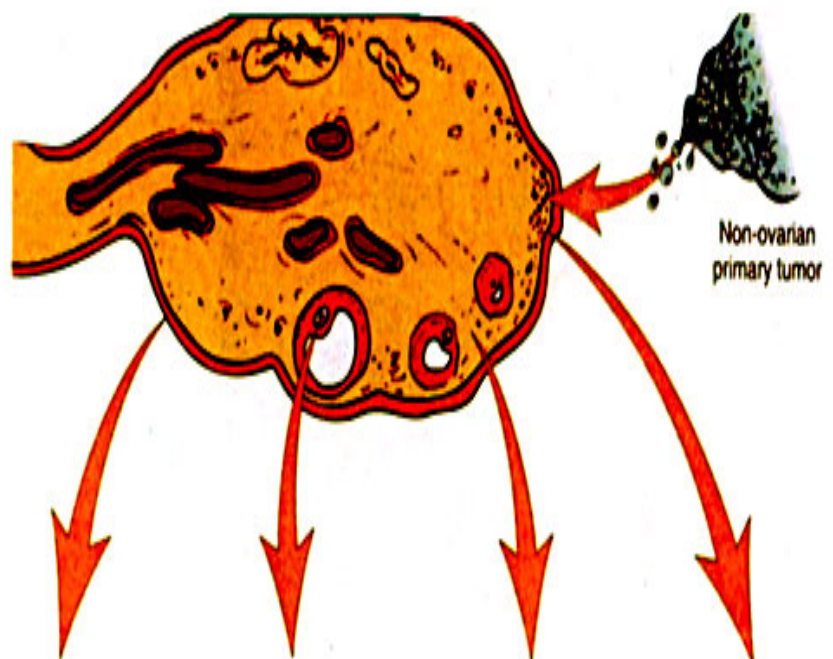
- Increased mitotic activity and nuclear atypia
- No stromal invasion
- Epithelial hyperplasia in the form of tufting, pseudostratification, cribriform and micropapillary structure
- Detached cell clusters

Most commonly ovarian tumor fall into three major categories - surface epithelial ovarian tumors, germ cell tumors and sex cord stromal tumor. They are usually asymptomatic, more than two third of the cases present in an advanced stage. Of all the gynaecological cancer it has the highest fatality to case ratio. It is the fifth most common cause of death from malignancy in women.

Around 75- 80% of ovarian tumors are epithelial in origin. Among them, 80% are benign and 20% are malignant. Around 80% of malignant ovarian tumors arise primarily from ovary, rest of the 20% arise either from GIT, breast or colon.

The classification of ovarian tumor (benign and malignant) is devised by world health organization according to the most probable tissue of origin ( scully 1999)

1. Surface epithelial (65% -75%)
2. Germ cell (15%)
3. Sex cord - stromal (10%)
4. Metastases (5%) & miscellaneous



ORIGIN	SURFACE EPITHELIAL CELLS (Surface epithelial-stromal cell tumors)	GERM CELL	SEX CORD-STROMA	METASTASIS TO OVARIES
Overall frequency	65%-70%	15%-20%	5%-10%	5%
Proportion of malignant ovarian tumors	90%	3%-5%	2%-3%	5%
Age group affected	20+ years	0-25+ years	All ages	Variable
Types	<ul style="list-style-type: none"> <li>• Serous tumor</li> <li>• Mucinous tumor</li> <li>• Endometrioid tumor</li> <li>• Clear cell tumor</li> <li>• Brenner tumor</li> <li>• Cystadenofibroma</li> </ul>	<ul style="list-style-type: none"> <li>• Teratoma</li> <li>• Dysgerminoma</li> <li>• Endodermal sinus tumor</li> <li>• Choriocarcinoma</li> </ul>	<ul style="list-style-type: none"> <li>• Fibroma</li> <li>• Granulosa-theca cell tumor</li> <li>• Sertoli-Leydig cell tumor</li> </ul>	

## **SURFACE EPITHELIAL - STROMAL TUMORS**

### **Serous tumors:**

- \* Benign (cystadenoma)
- \* Borderline tumors (serous borderline tumor)
- \* Malignant (serous adenocarcinoma)

### **Mucinous tumors, endocervical-like or intestinal type:**

- \* Benign (cystadenoma)
- \* Borderline tumors (mucinous borderline tumor)
- \* Malignant (mucinous adenocarcinoma)

### **Endometrioid tumors:**

- \* Benign (cystadenoma)
- \* Borderline tumors (endometrioid borderline tumor)
- \* Malignant (endometrioid adenocarcinoma)

### **Clear cell tumors:**

- \* Benign
- \* Borderline tumors
- \* Malignant (clear cell adenocarcinoma)

**Transitional cell tumors:**

- \* Brenner tumor
- \* Brenner tumor of borderline malignancy
- \* Malignant Brenner tumor
- \* Transitional cell carcinoma (non-Brenner type)

**Epithelial-stromal**

- \* Adenosarcoma
- \* Carcinosarcoma (formerly mixed Muellarian tumors)

**SEX CORD - STROMAL TUMORS****Granulosa tumors:**

- \* Fibromas
- \* Fibrothecomas
- \* Thecomas

**Sertoli cell tumors:**

- \* Leydig cell tumors
- \* Sex cord tumor with annular tubules
- \* Gynandroblastoma
- \* Steroid (lipid) cell tumors



## **Germ cell tumors**

### **Teratoma:**

- \* Immature
- \* Mature
- \* Solid
- \* Cystic (dermoid cyst)

### **Dysgerminoma**

### **Endodermal sinus tumor**

### **Embryonal carcinoma**

### **Polyembryoma**

### **Choriocarcinoma**

### **Mixed forms**

### **Monodermal (e.g., struma ovarii, carcinoid)**

### **Yolk sac tumor (endodermal sinus tumor)**

### **Mixed germ cell tumors**

## **MALIGNANT, NOT OTHERWISE SPECIFIED**

### **Metastatic cancer from nonovarian primary:**

- \* Colonic, appendiceal
- \* Gastric
- \* Breast

### **SEROUS TUMORS:**

Serous tumors are the most common epithelial ovarian tumor constituting 50% of all epithelial tumors. Benign serous tumors accounting for approximately 60-70% , while malignant tumors constitute 20-25% and borderline constitute 15%.

Serous benign tumors occur in 4<sup>th</sup> and 5<sup>th</sup> decade of life. The cyst is lined by flattened epithelial cells that resembles fallopian tube lining, filled with straw coloured fluid, may have a few coarse papillary projections, occur between 30 and 50yrs of age.

Borderline serous tumors occur in 5<sup>th</sup> decade of life. They have finer papillary projections within the cyst cavity.the external surface of the tumor also have similar projections. In upto 40% of the patients. Similar tumorlets may also found the pelvis and abdominal cavity.5 year survival rate is around 70-95%.Recurrences usually develop after 20-50years in pelvic and abdominal cavity.

Malignant tumors are usually multiloculated, partially cystic, and may also contain solid areas occur in 6<sup>th</sup> decade of life. They have an abundance of delicate papillary projections. Two third of them are bilateral. With stage I tumor, 5 year survival rate is found to be 76% ,56% for stage II ,25% stage III and for patients with stage IV ovarian tumors it is around 9%.

### **MUCINOUS OVARIAN TUMOR:**

Mucinous tumors are formed by cells that are similar to intestinal or endocervical epithelium. They constitute 15-25% of epithelial ovarian tumor. Benign tumors are usually unilateral, multiloculated occurring between the third and fifth decade of life. Borderline tumors resembles benign tumors but may have solid areas and papillary projections occur in fourth and sixth decade of life or more 15-25% of epithelial tumor. They are mostly unilateral and usually multiloculated cystic tumor. They may reach upto 30cm size. The cyst wall is smooth and filled with thick mucinous fluid. Most of them are benign, while 10-15% constitute borderline tumor, and 5-10% are malignant. Malignant tumors have more papillary projections within the cyst cavities, larger solid areas, larger areas of necrosis and haemorrhage. Occur in sixth decade of life. With stage I tumor the 5 year survival rate is found to be 83%, and for patients

with stage II tumors it is 55%, for stage III it is around 21% and for stage IV tumors it is 9%.

Pseudomyxoma peritonei, results from tumor of intestinal type which ruptures and leads to dense adhesions. However most cases are found to arise from mucinous tumors that are primary to appendix.

### **ENDOMETRIOID OVARIAN TUMORS:**

These are ovarian tumors formed by cells that resemble endometrial lining. They may be associated with endometriosis (15%), endometrial hyperplasia, or endometrial carcinoma (20%).

Both Benign and borderline tumors usually occur in 6<sup>th</sup> decade of life and are mostly cystic and unilateral. These tumors have an excellent prognosis.

Malignant tumors are predominantly solid and constitutes 80% of ovarian endometrioid tumors 10-25% of all ovarian cancer. They have better prognosis as compared to serous and mucinous tumors. The 5 year survival rate is 78% for stage I, 63% for stage II tumors, for stage III - 24% and for stage IV tumors 6%.

## **CLEAR CELL TUMORS:**

Clear cell ovarian tumors, also known as mesonephroid tumor are formed by hob nail like cells. Clear cell tumors are usually malignant, predominantly solid or cystic with polypoidal mass protruding into them. They constitute 4-5% Of all malignant ovarian tumors, and 50-60% of them have endometriosis. They have poorer survival rate when compared to other surface epithelial ovarian tumors.

## **BRENNER TUMOR:**

Brenner, formed by cells that resemble lining of bladder (urothelium). It is a rare tumor constituting 2-3% of all epithelial tumors. these tumors are usually small, predominantly solid, and unilateral. “Walhard cell nests” is characteristic of Brenner tumor. Due to the presence of longitudinal groove these cells have puffed wheat appearance. Mucinous tumorare often associated with brenner. Occasionally, pseudomeig syndrome presents with Brenner.

## **GERM CELL TUMORS:**

Germ cell tumors tend to develop in children and adolescents. One third of these tumors are malignant. In adults germ cell tumors are rare, majority of them being mature cystic teratoma.

- Teratoma
- Dysgerminoma

- Endodermal sinus tumor(yolk sac tumor)
- Choriocarcinoma

They constitute 15-20% of all ovarian tumors, of which 95% of them are benign cystic teratoma.

### **TERATOMA:**

Teratoma are formed by cells derived either from ectoderm, endoderm or mesoderm. It can be mature teratoma (dermoid Cyst), Benign Immature teratoma, malignant (Monodermal highly specialised tumor – struma ovarii).

### **Benign cystic teratoma:**

Mature or benign teratomas can be either solid or cystic. Benign cystic teratoma is also known dermoid cyst. It is the most common ovarian germ cell tumor. Ectodermal cells predominate in most of the mature cystic teratoma. They usually have a cyst filled with sebaceous material, often have teeth, hair, bone or cartilage. Most commonly occur during reproductive years. Rarely they may undergo malignant transformation particularly in postmenopausal women. Prognosis is very poor with 5 year survival rate being only 15-31%.

These tumors are usually unilateral, grows slowly, but found to be large at the time of diagnosis.

**Immature teratoma:**

They are the second most common germ cell tumor. It is usually unilateral, large and predominantly solid. They usually have a malignant behavior, grows rapidly, spread by implantation throughout the peritoneal cavity. Lymphatic system is the primary channel for metastasis. Recurrence occurs following surgery, but combination chemotherapy leads to permanent remission.

**Struma Ovarii :**

These tumor contain specialised monodermal tissue particularly thyroid tissue. Hyperthyroidism occurs in 5-8% of patients with struma ovarii. Here the thyroid cells develop at the expense of other tissues. Most of them are benign but malignant transformation may occur.

**Carcinoid:**

Carcinoid another form of monodermal specialised tumor. It can be either primary or secondary. It is also known as Argentaffinoma. It secretes hydroxy tryptamine which causes flushing and cyanosis.

**DYSGERMINOMA:**

Dysgerminoma is the most common malignant germ cell tumor, similar to their testicular counterpart seminoma occurs in 2<sup>nd</sup> and 3<sup>rd</sup> decade of life. Usually unilateral and 10-20% of them bilateral.

These tumors are usually solid, composed of clear round cells. They secrete high level of Lactate dehydrogenase and can be used as tumor marker. Clear round cells along with lymphocytic infiltration are characteristic feature of dysgerminoma. Metastasis occurs in an advanced stage of the disease through lymphatic system. These tumors are radiosensitive. Prognosis is good with the 5 year survival rate being 100% for stage I patients, 75-90% for patients with other stage of the disease. However, large tumor, bilaterality, <20 years or >20 year are associated with poor prognosis.

#### **ENDODERMAL SINUS TUMOR (YOLK SAC TUMOR):**

The cellular structures of these tumors are similar to the primitive yolk sac. These are predominantly solid but may have cystic spaces. They are highly malignant, invading the surrounding structures. Metastasis occur early particularly through lymphatic system. Usually unilateral, involvement of the opposite is the evidence of metastasis. Usually secrete alpha fetoprotein that can be used as a tumor marker. Radiotherapy is ineffective, most cases can be cured with surgery followed by multiagent chemotherapy.

#### **EMBRYONAL CELL CARCINOMA:**

Embryonal cell carcinoma is a highly malignant, tend to occur in combination with yolk sac tumor. Usually unilateral, solid, large, have



variegated appearance occur in children and young adults secrete AFP and HCG, and the latter is responsible for precocious puberty and abnormal uterine bleeding. Metastasis occurs early through lymphatic system. Tumors are radio insensitive, but treatment with surgery and chemotherapy cures most of the patients.

### **CHORIOCARCINOMA:**

Ovarian choriocarcinoma, rare form, formed by placental elements. They are usually solid, unilateral and have a haemorrhagic appearance. Majority of the primary tumors are not related to pregnancy, some may occur after pregnancy, in which case most are metastatic. They secrete HCG, hence HCG hormonal assay may be used as a tumor marker. They are invasive locally, and metastasis early. Gestational choriocarcinoma spread through blood stream whereas non gestational tumors by lymphatic system.

### **SEX CORD STROMAL TUMOR:**

Sex cord stromal tumor constitutes 8% of all ovarian tumors and 7% of all malignant ovarian tumors. Endocrine manifestations are often associated with these tumors.

## **GRANULOSA CELL TUMOR:**

Granulosa cell tumors are formed by cells derived from germinal cells in ovarian follicles. Granulosa cell tumor occur in adult form and juvenile form. Adult GCT are partially cystic with blood filled loci, and solid areas. Most of them are unilateral, slow growing tumor occur in postmenopausal women. Most commonly associated with overproduction of ovarian hormones resulting in estrogenic manifestations (endometrial hyperplasia, endometrial cancer). Treatment is primarily surgical, Juvenile GCT are similar to adult one, constitute only 5% of granulosa cell tumor. Majority of them are unilateral, and about half of them occur before puberty, resulting in precocious sexual development due to production of estrogen from the tumor. surgical excision is curative.

Due to its lipid content it will be yellow or orange in cut section. In histopathological examination, cells resemble granulosa cells, with characteristic formation of Call Exner body. Coffee bean appearance is pathognomonic of granulosa cell tumor.

The tumor cells also secrete inhibin which can be used as a tumor marker. Metastasis first spreads to opposite ovary followed by lumbar region then later on to liver, mesentery and the mediastinum.

**THECA CELL TUMOR:**

Theca cell tumor is a rare, solid tumor formed by theca cells which resembles cells that surrounds the ovarian follicles. They are usually unilateral, occur in postmenopausal women with the manifestation of postmenopausal bleeding, endometrial cancer, endometrial hyperplasia. Most of them are benign and surgery is curative.

**ARRHENOBLASTOMA:**

These are rare tumors which secretes androgens and cause masculinization. Arrhenoblastoma when develops in child bearing age group results in alteration of body contour, irregularity of menstruation, resulting in amenorrhea. Later, they may develop cliteromegaly, hirsutism, and finally with breakup of voice. These tumors are usually unilateral with high malignant potential. In HPE, the tumor shows seminiferous tubules.

**GYNANDROBLASTOMA:**

Gynandroblastoma, is a rare, benign tumor with combination of both granulosa cell tumor and arrhenoblastoma.

**GONADOBLASTOMA:**

Gonadoblastoma is a rare tumor often associated with dysgerminoma.

### **OVARIAN FIBROMA:**

The spindled stromal cells give rise, solid ovarian tumor, fibroma. Usually occur after 30 years of age. These tumors often benign and cured by surgical treatment. Usually unilateral, rarely bilateral, and may be associated with nevoid basal cell carcinoma (also called Gorlin syndrome).

Ovarian fibroma is commonly associated with Brenner tumor. Ovarian fibroma along with right sided pleural effusion and ascites is known as Meigs syndrome.

### **METASTATIC (SECONDARY) CARCINOMA OF OVARY:**

Secondaries of ovary develop with primary elsewhere in the body, and they constitute around 20%. Most common of them are from GIT, and uterus and cervix.

There are two types of secondary carcinoma. In the first one, the secondaries get deposited over the ovary either by direct spread or by lymphatic permeation. These tumors are usually bilateral with bosselated appearance often associated with ascites and peritoneal deposits.

Second one is the Krukenberg tumor. These tumors are often bilateral with smooth surface and intact capsule and larger than the

primary tumor. Signet ring cell is characteristic of krukensberg tumor .Pylorus, colon and breast being the most common primary site. The mode of spread is by retrograde lymphatics.

## **MATERIALS AND METHODS**

This prospective study was performed in the Department of Obstetrics and gynaecology, Tirunelveli Medical College and hospital. The study was conducted during the period 2012 to 2014. The study population consisted of 100 patients who were admitted in our hospital with adnexal masses.

### **INCLUSION CRITERIA**

Patients above the age of 25 years admitted in our hospital both in premenopausal and postmenopausal age group with a diagnosis of an ovarian mass were included in the study.

### **EXCLUSION CRITERIA**

Ovarian mass in the pregnant women were excluded because CA 125 levels will be elevated in pregnancy and hence may give a false positive result.

Patients with previously diagnosed disease commonly associated with elevated CA 125 levels were excluded. Patients on peritoneal dialysis which by constant peritoneal irritation cause an elevated CA 125 levels and are therefore exclude from the study.

This study was performed after Institutional ethical committee approval. The objective of the study was explained in detail and written consent was obtained from the patients included in the study. Serum CA 125 and the ultrasound examination were performed at the time of preoperative laboratory assessment which was usually accomplished approximately within 1 week prior to surgery.

Serum CA 125 was determined by radioimmunoassay.

Ultrasound examination was performed using a 3.5-MHz abdominal convex transducer in patients with full bladder or 7.5-MHz vaginal probe in patients after emptying the bladder. Ultrasound score was assigned for the following features.

1. Multiloculations,
2. Presence of solid elements,
3. Bilaterality,
4. Presence of ascites, or
5. Evidence of metastases.

An ultrasound score (U) of 1 was given if none or one of the features was found, and a score of 3 was given if two or more of these features were shown. Postmenopausal status was defined as more than one year of amenorrhea or age older than 50 years for women who had

undergone hysterectomy; they were scored as M=3. All other patients who did not meet these criteria were defined in a premenopausal status which scored M=1. The absolute values of serum CA-125 was entered in formula.

Ultrasonographic examination of pelvic organs was performed, menopausal status and level of cancer antigen 125 (CA125) were assessed and finally RMI was calculated for all the patients. RMI was calculated using the formula:

$$\text{RMI SCORE} = \text{Ultrasound score} \times \text{menopausal score} \times \text{CA125 level in U/ml}$$

After surgery, histopathological (HPE) findings of excised tumors were analysed in order to determine the final diagnosis. The histopathological diagnosis is considered as the gold standard for defining the outcomes finally, based on the standard formulas, sensitivity, specificity, positive predictive value and negative predictive value of the RMI was calculated, as RMI is an index which indicates malignancy with reference to the actual presence or absence of malignancy in the ovarian mass.



**SENSITIVITY :**

The sensitivity is defined as the percentage of patients with malignant ovarian mass having a positive test result.

$$\text{Sensitivity} = [(\text{true positive} / \text{true positive} + \text{false negative}) \times 100]$$

**SPECIFICITY :**

The specificity is defined as the percentage with benign ovarian mass showing negative results.

$$\text{Specificity} = [(\text{true negative} / \text{true negative} + \text{false positive}) \times 100]$$

**POSITIVE PREDICTIVE VALUE :**

The positive predictive value is defined as the percentage of patients with a positive test result having malignant ovarian mass.

$$\text{Positive predictive value} = [(\text{true positive} / \text{true positive} + \text{false positive}) \times 100]$$

**NEGATIVE PREDICTIVE VALUE :**

The negative predictive value is defined as the percentage of patients with a negative test result having benign ovarian mass.

$$\text{Negative predictive value} = [(\text{true negative} / \text{true negative} + \text{false negative}) \times 100]$$

## **STATISTICAL ANALYSIS :**

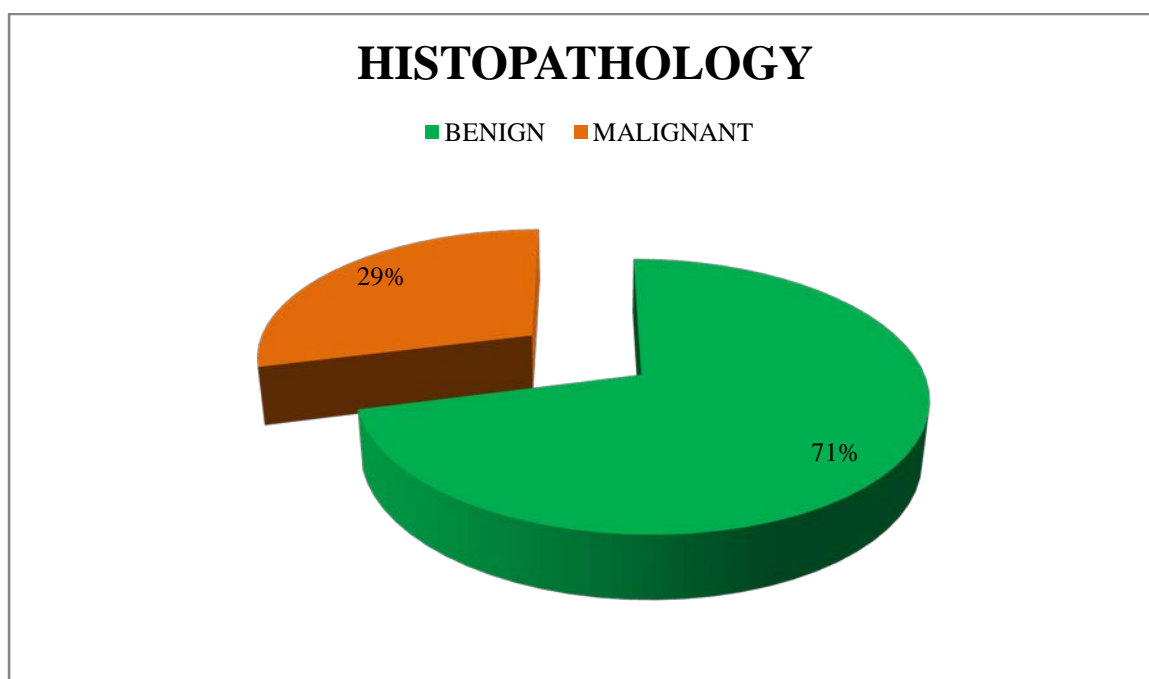
Data were analyzed using chi-square tests. Descriptive statistics were used for demographic data and summarized as mean with standard deviation or frequency with percentage. Univariate analyses to determine the association of each parameter were performed using Student's t test. The independent association was then determined by logistic regression. The diagnostic performances of each test were reported as sensitivity, specificity, positive predictive value, and negative predictive value with 95% confidence interval.

## OBSERVATION & RESULTS

**TABLE 1**

HISTOPATHOLOGY	NO OF PATIENTS	PERCENTAGE
BENIGN	71	71%
MALIGNANT	29	29%

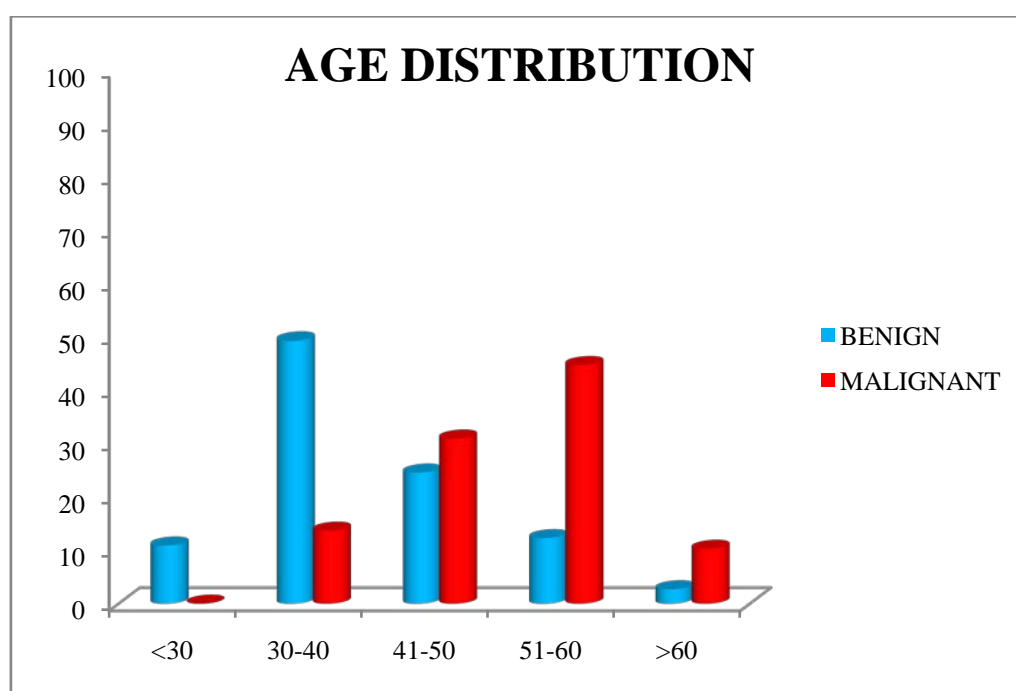
The study included 100 patients with ovarian mass of which 71 patients have benign tumor and 29 patients have malignant ovarian tumor.



## AGE DISTRIBUTION

	<30	30-40	41-50	51-60	>60
BENIGN	(8)10.9%	(35)49.3%	(17)24.6%	(09)12.3%	(02)2.7%
MALIGNANT	(0)0	(04)13.7%	(09)31%	(13)44.8%	(03)10.3%

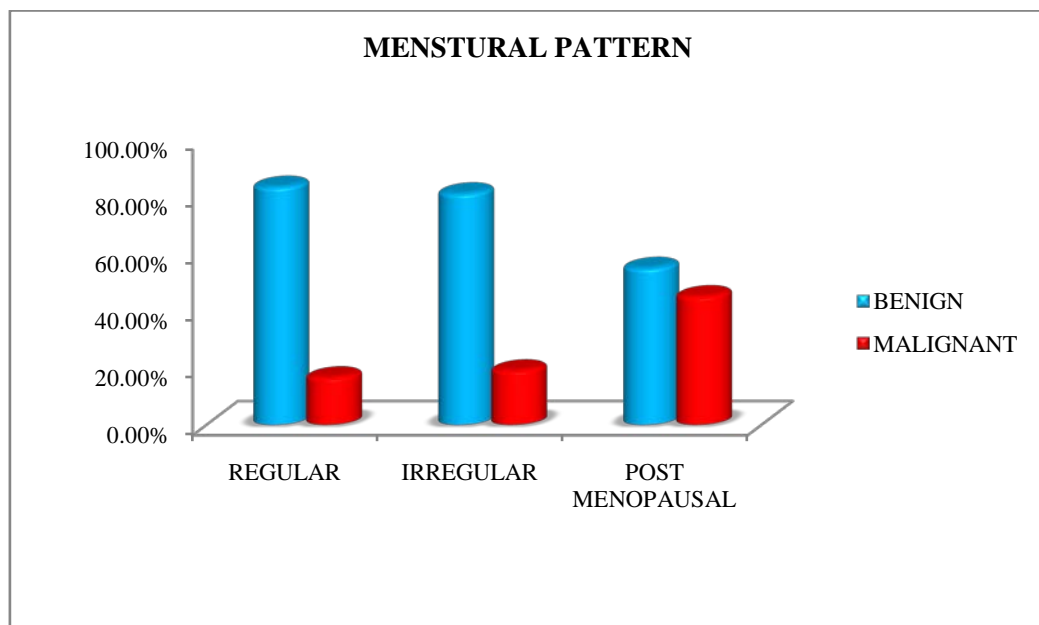
In the age group of 51-60 yrs of age 44.8% of cases are malignant whereas in 30-40 yrs of age only 13.7% are malignant. The percentage of malignant ovarian tumor increases with increase in age group.



## MENSTURAL HISTORY

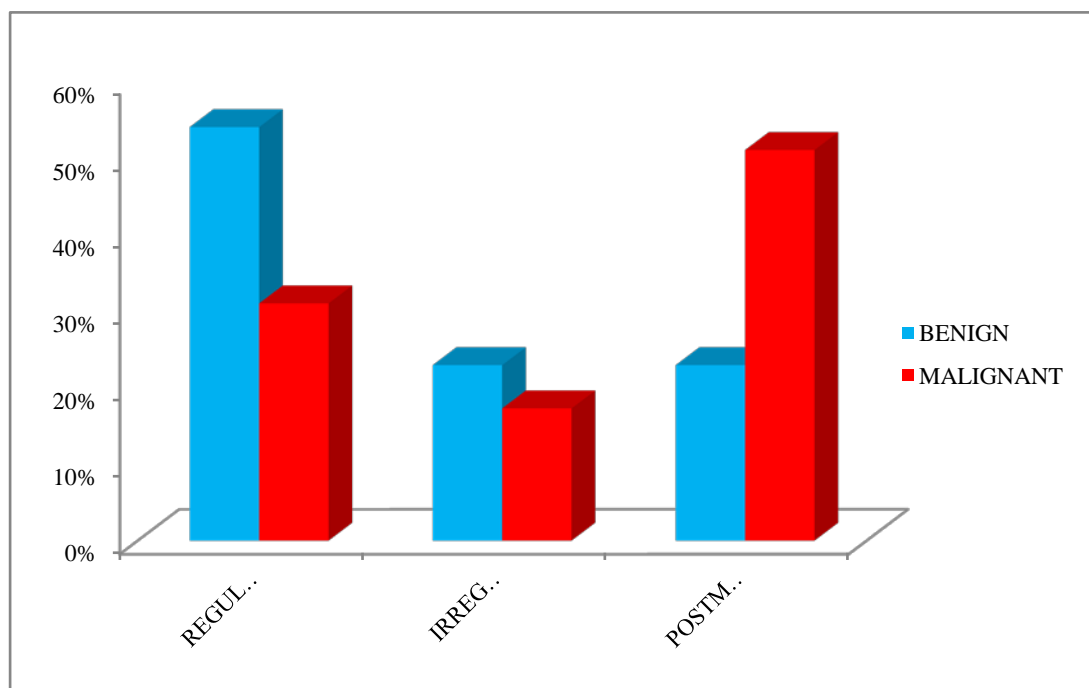
	<b>BENIGN</b>	<b>MALIGNANT</b>
REGULAR	(39)83.30%	(09)16.60%
IRREGULAR	(16)80.95%	(05)19.04%
POST MENOPAUSAL	(16)54.80%	(15)45.10%

In this study among the postmenopausal women, nearly half of the patients have malignant ovarian tumor, 16.6% of patients with regular cycles and 19% of the patients with irregular cycles have malignant ovarian tumor.



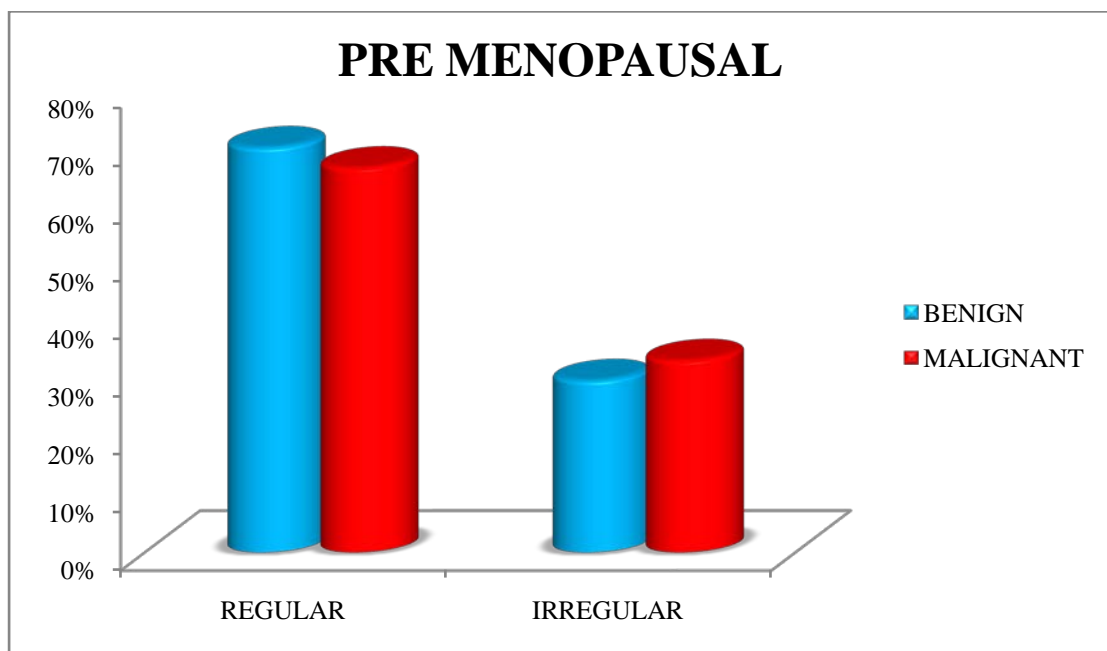
<b>HPE</b>	<b>REGULAR</b>	<b>IRREGULAR</b>	<b>POST MENOPAUSAL</b>
BENIGN	(39)54%	(16)22.90%	(16)22.90%
MALIGNANT	(09)31%	(05)17.24%	(15)51%

In this study, among the patients with malignant ovarian tumor n=29, 51% of the patients belong to postmenopausal age group whereas 22.90% of the women with benign tumor are in postmenopausal age group.



<b>PRE MENOPAUSAL</b>	<b>REGULAR</b>	<b>IRREGULAR</b>
<b>BENIGN</b>	(39)70%	(16)29.82%
<b>MALIGNANT</b>	(09)6.60%	(05)33.30%

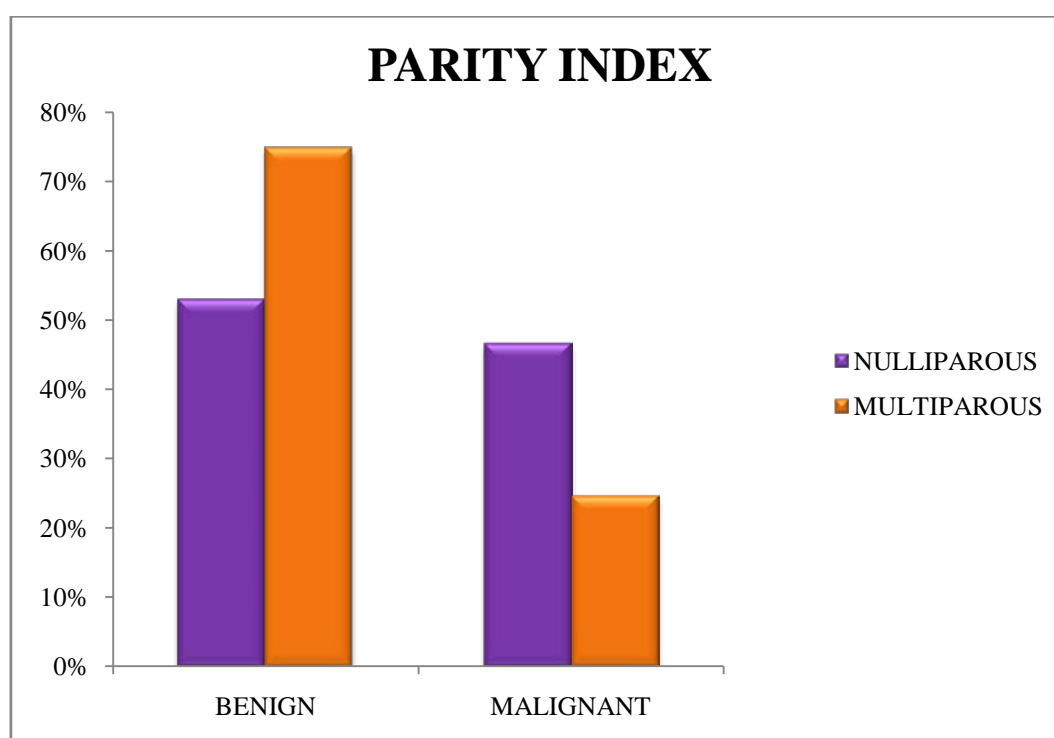
Among 69 patients in premenopausal age group 70% of patients with benign tumor have regular cycles whereas the remaining have irregular cycles .6.6% of patients with malignant ovarian tumor have regular cycles and 33.3% have irregular cycles .



## PARITY INDEX

PARITY INDEX	BENIGN,(n) %	MALIGNANT,(n)%
NULLIPAROUS	(08)53%	(07)46.60%
MULTIPAROUS	(63)75%	(22)24.70%

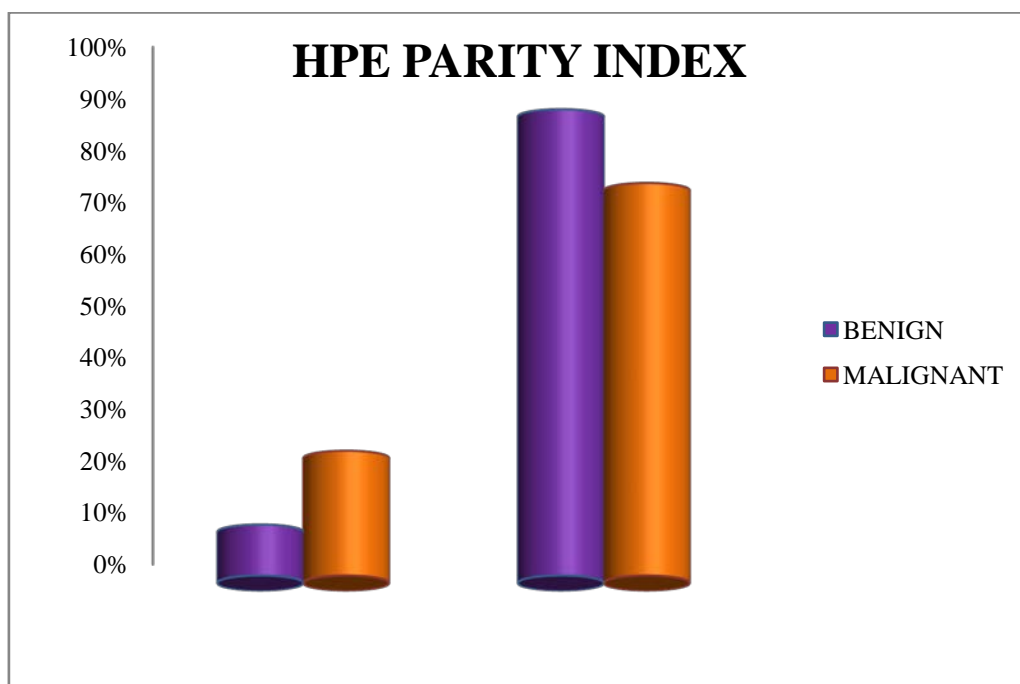
In our study 15 patients are nulliparous and 85 patients are multiparous women. In nulliparous women 53% have benign ovarian tumor, whereas 46% have malignant ovarian tumor. Among multiparous women 75% have benign and 24% have malignant ovarian tumor.





<b>HPE</b>	<b>NULLIPAROUS</b>	<b>MULTIPAROUS</b>
<b>BENIGN</b>	(8)10%	(63)90.14%
<b>MALIGNANT</b>	(7)24.13%	(22)75.86%

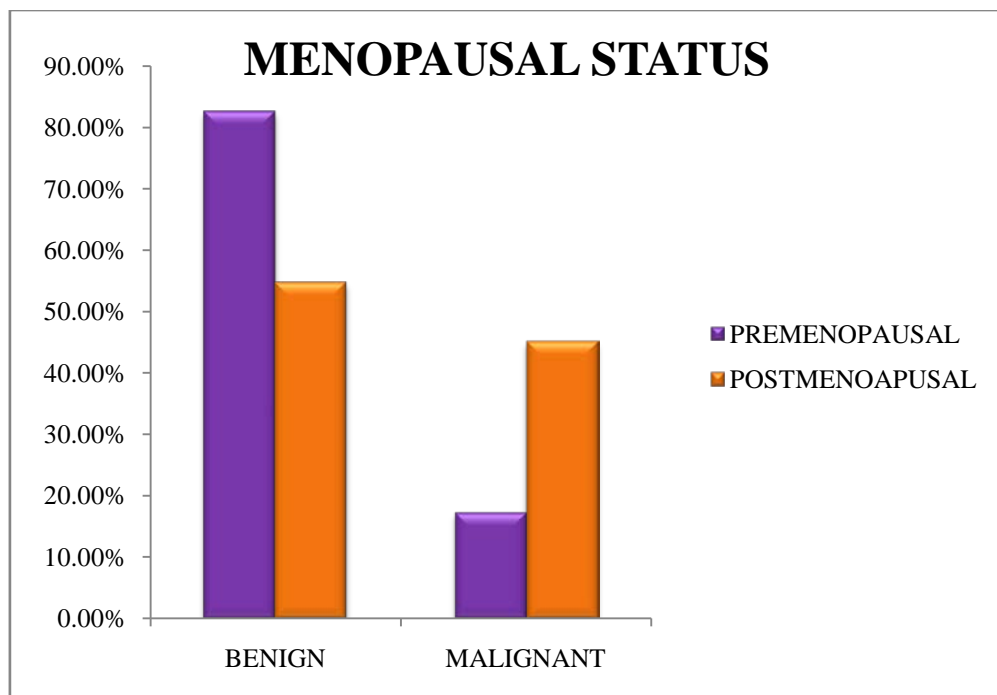
Among the patients with benign tumors, 10% are nulliparous and 90% are multiparous and among patients with malignant tumors 24% are nulliparous and 75.86% are multiparous.



## MENOPAUSAL STATUS

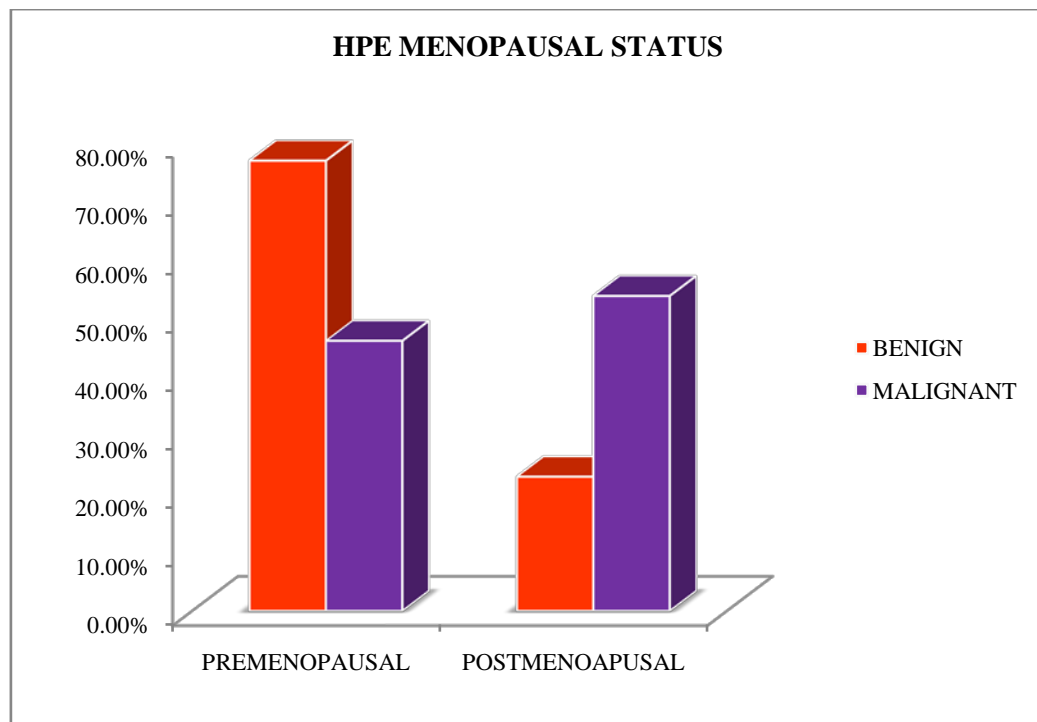
	<b>BENIGN</b>	<b>MALIGNANT</b>
<b>PREMENOPAUSAL</b>	(55)82.60%	(14)17.39%
<b>POSTMENOAPUSAL</b>	(16)54.83%	(15)45.16%

In our study 69 patients are in premenopausal age group and 31 patients are in postmenopausal age group. Among 69 premenopausal patients 55 have benign tumor accounting for 82.6% and 14 have malignant tumor accounting for 17.39%. Among 31 postmenopausal patients 16 have benign tumor accounting for 54.83% and 15 patients have malignant ovarian tumor accounting for 45.16%



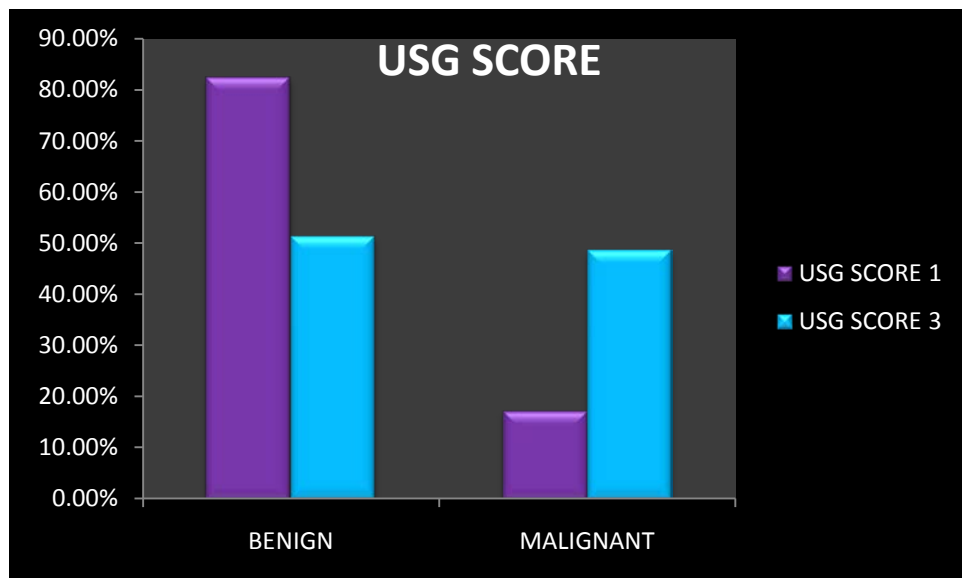
<b>HPE</b>	<b>PREMENOPAUSAL</b>	<b>POSTMENOAPUSAL</b>
<b>BENIGN</b>	(55)77.02%	(16)22.97%
<b>MALIGNANT</b>	(14)46.15%	(15)53.84%

Among 71 benign tumors, 77.02% of patients are in premenopausal age group and 22.97% in postmenopausal age group .Among 29 patients with malignant tumors 46.15% are in premenopausal age group and 53.84% are in postmenopausal age group. Sensitivity, specificity, positive predictive value and negative predictive value of menopausal score are 53.84%,77.02% ,45.61% and,82.61%, respectively.



USG SCORE	BENIGN	MALIGNANT
USG SCORE 1	(52)82.53%	(11)17.46%
USG SCORE 3	(19)51.35%	(18)48.64%

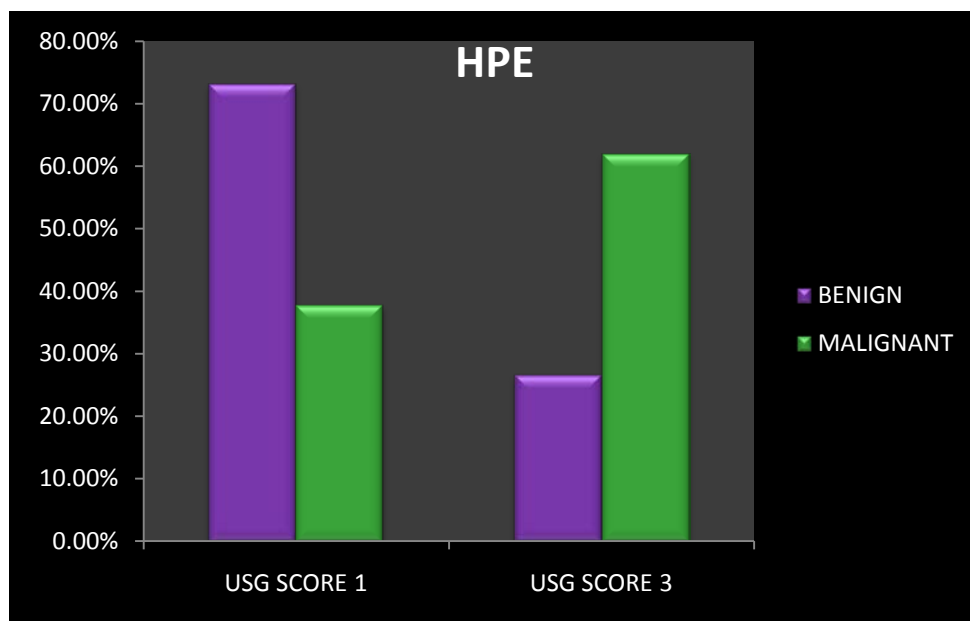
In this study, 63 Patients have ultrasound score of 1, that is presence of one or none of the parameters in ultrasound. Among 63 patients, 82.53% have benign lesions and 17.46% patients have malignant ovarian tumor. 27 patients have ultrasound score of 3 indicating presence of 2 or more parameters of ultrasound criteria. Among Patients with ultrasound score of 3, 51.35% have benign lesions and 48.64% have malignant ovarian tumor .



HPE	USG SCORE 1	USG SCORE 3
BENIGN	(52)73.23%	(19)26.76%
MALIGNANT	(11)37.93%	(18)62.06%

On analysis, among benign tumors 73.23% have ultrasound score of 1 and 26.76% have ultrasound score of 3. Among malignant ovarian tumor 37.93% have ultrasound score of 1 and 62% have ultrasound score of 3.

The performance status of ultrasound score has been analysed with sensitivity of 62.06%, specificity of 73.23%, positive predictive value of 48.64% and negative predictive value of 82.54% respectively.

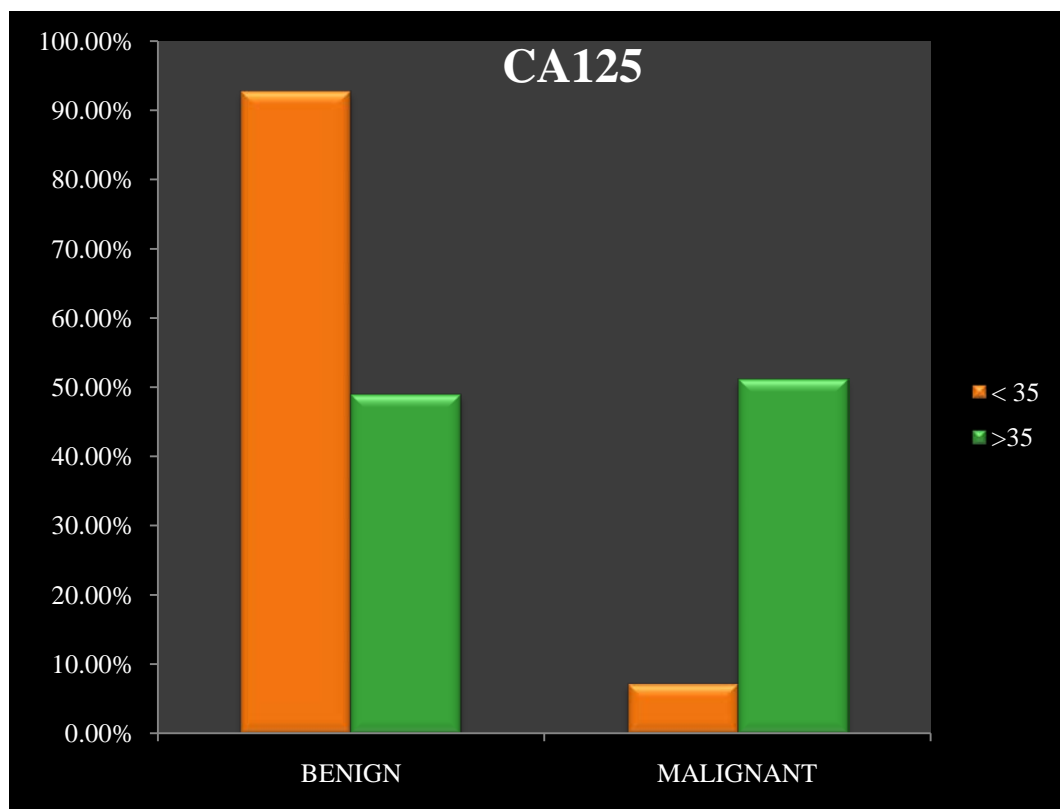


### CA 125-CUT OFF 35

CA125	BENIGN	MALIGNANT
< 35	(50)92.72%	(05)7.27%
>35	(21)48.88%	(24)51.11%

CA 125 is analysed with cut off value of 35U/ml. Normal range is 0-35U/ml. In our study, CA 125 with cut off value of 35U/ml 45 patients have >35U/ml.

Among them 48% have benign lesions and 51% have malignant lesions. 92.72% of patients with CA 125 <35U/ml have benign lesions and 7.27% have malignant lesions.



<b>HPE</b>	<b>&lt; 35</b>	<b>&gt;35</b>
<b>BENIGN</b>	(40)69.86%	(31)30.13%
<b>MALIGNANT</b>	(05)14.81%	(24)85.18%

SENSITIVITY-85.18%

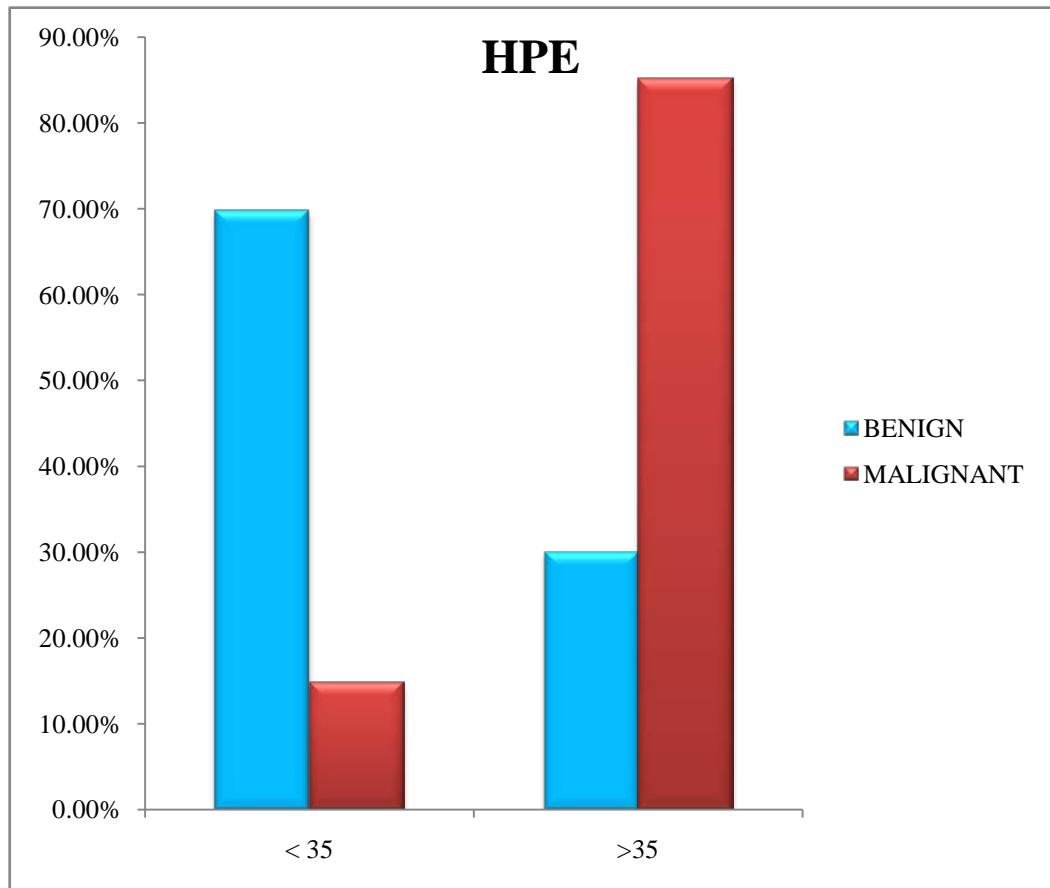
SPECIFICITY-69.86%

POSITIVE PREDICTIVE VALUE -51.11%

NEGATIVE PREDICTIVE VALUE-92.73%

Among patients with benign tumor, 69.85% have CA 125< 35U/ml and 30.13% have CA 125 > 35U/ml whereas the patients with malignant ovarian tumor 14.8% have CA 125 <35 and 85.18% have CA 125 >35U/ml.



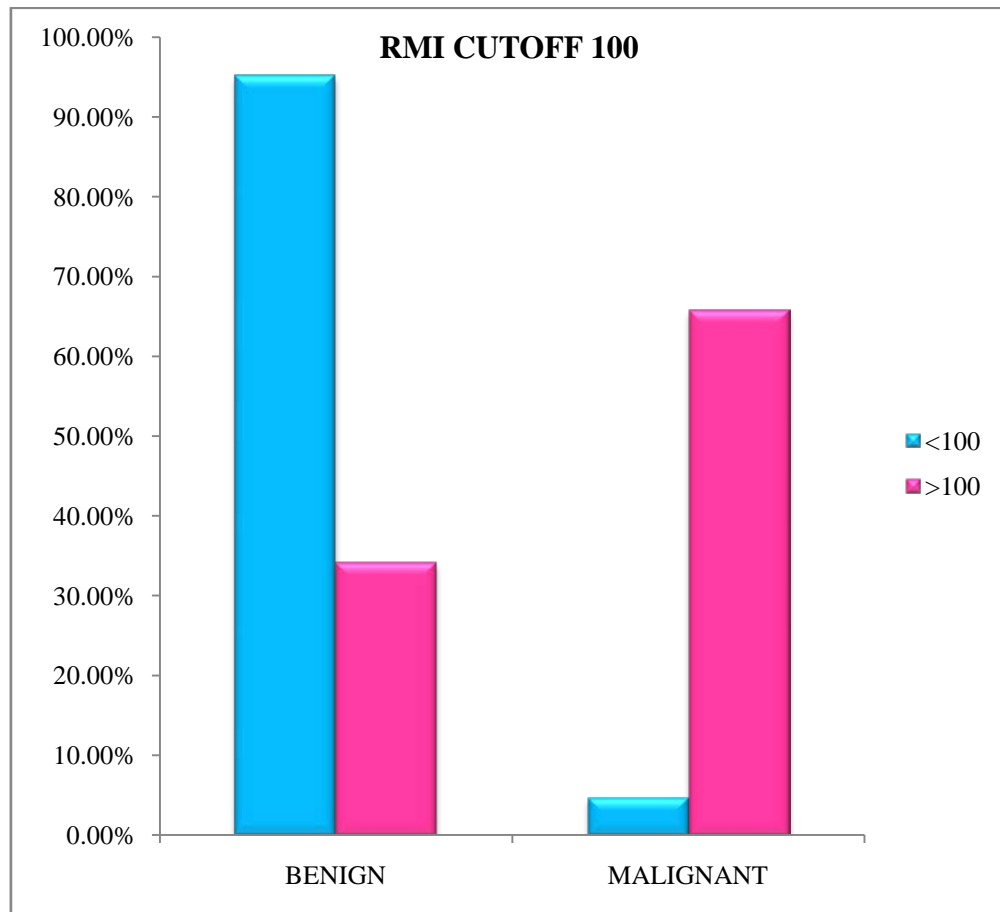


### **RMI- CUT OFF 100**

<b>RMI CUT OFF 100</b>	<b>BENIGN</b>	<b>MALIGNANT</b>
<100	(59)95.16%	(03)4.83%
>100	(12)34.21%	(26)65.78%

The risk of malignancy index based on USG score, CA -125 and menopausal status was calculated preoperatively. With the cut off value of 100, 62 patients are below 100 and 38 patients are above 100. 95.16% of patient with RMI <100 have benign tumor and 65.78% of patients with RMI >100 have malignant tumor. 81.94% of patients with benign tumor have RMI <100 and 89.24% of patients with malignant tumor have RMI > 100.

The sensitivity of RMI with cut off point of 100 is 89.24%, specificity is 81.94%, positive predictive value is 65.79% and negative predictive value is 95.16%.

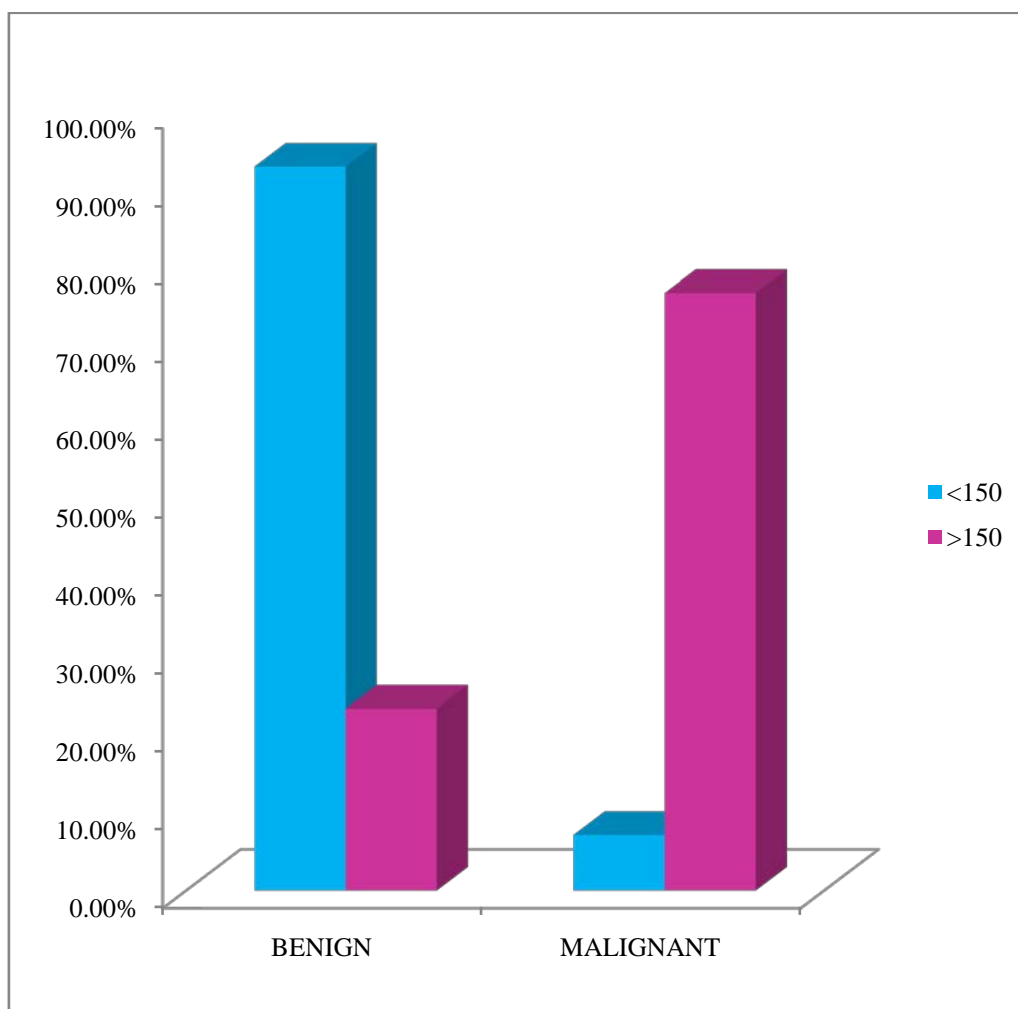


### **RMI - CUT OFF 150**

<b>RMI</b>	<b>BENIGN</b>	<b>MALIGNANT</b>
<150	(65)92.85%	(06)7.14%
>150	(06)23.33%	(23)76.66%

With the cut off value of RMI at 150, 71 patients have value below 150 and 29 patients have value above 150. Patients with RMI <150, 92.85% have benign lesions and 7.14% have malignant lesions. Those with RMI > 150, 23.33% have benign lesions and 76.66% have malignant lesions 7.14% of patients with benign tumors have RMI <150 and 76.66% of patients with malignant tumors have RMI >150.

With the cut off value of 150, sensitivity, specificity, positive predictive value and negative predictive value are 80%, 87.7%, 65.5% and 93.8% respectively.

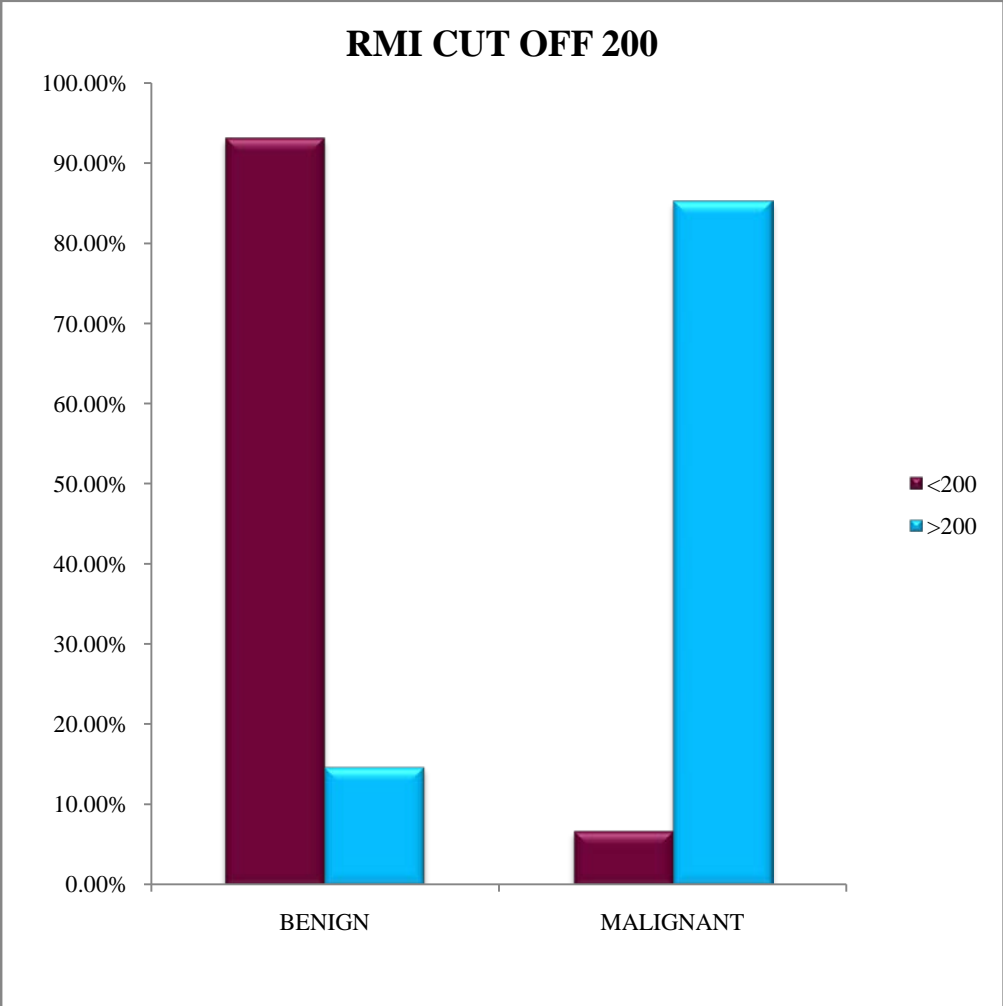


### **RMI CUT OFF 200**

<b>RMI CUT OFF 200</b>	<b>BENIGN</b>	<b>MALIGNANT</b>
<200	(68)93.15%	(05)6.84%
>200	(03)14.81%	(24)85.18%

In this study 73 patients have RMI value <200 and 27 patients have RMI >200. 93.15% and 6.84% of patients with RMI < 200 have benign and malignant tumor respectively .Those with RMI >200, 14.81% have benign lesions and 85.18% have malignant tumors.

The sensitivity of RMI with cut off value 200 is 82.14%, specificity is 94.44%, positive predictive value is 85.19%, negative predictive value is 93.15%.



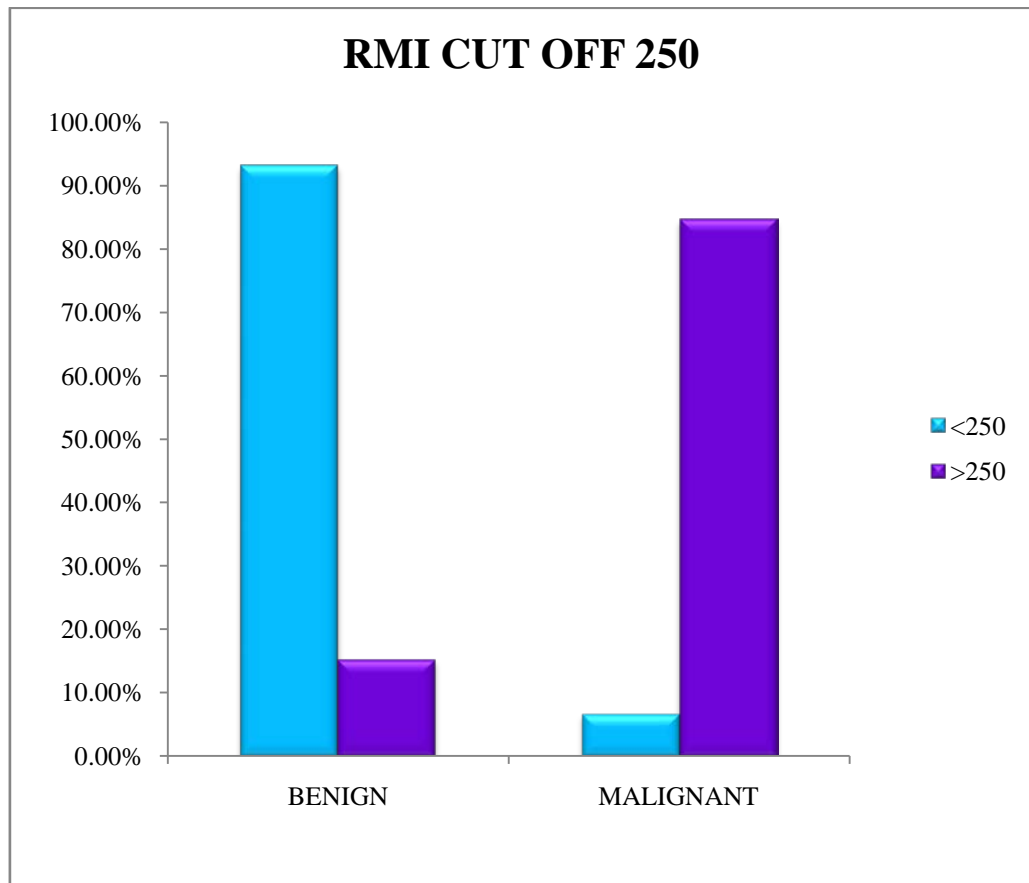
### **RMI CUT OFF 250**

<b>RMI CUT OFF 250</b>	<b>BENIGN</b>	<b>MALIGNANT</b>
<250	(68)93.24%	(05)6.75%
>250	(03)15.38%	(24)84.61%

If the RMI has the cut off value of 250, 73 patients have RMI <250 and 27 patients have RMI > 250. 93.24 % of patients with RMI <250 have benign lesion and 6.75% have malignant lesions.15.38% of patients with RMI> 250 have benign lesions and 84.61% of patients have malignant lesions.

With the cut off value of 250 sensitivity, specificity ,positive predictive value and negative predictive value are 81.48%, 94.52%, 84.62% and 93.24% respectively.

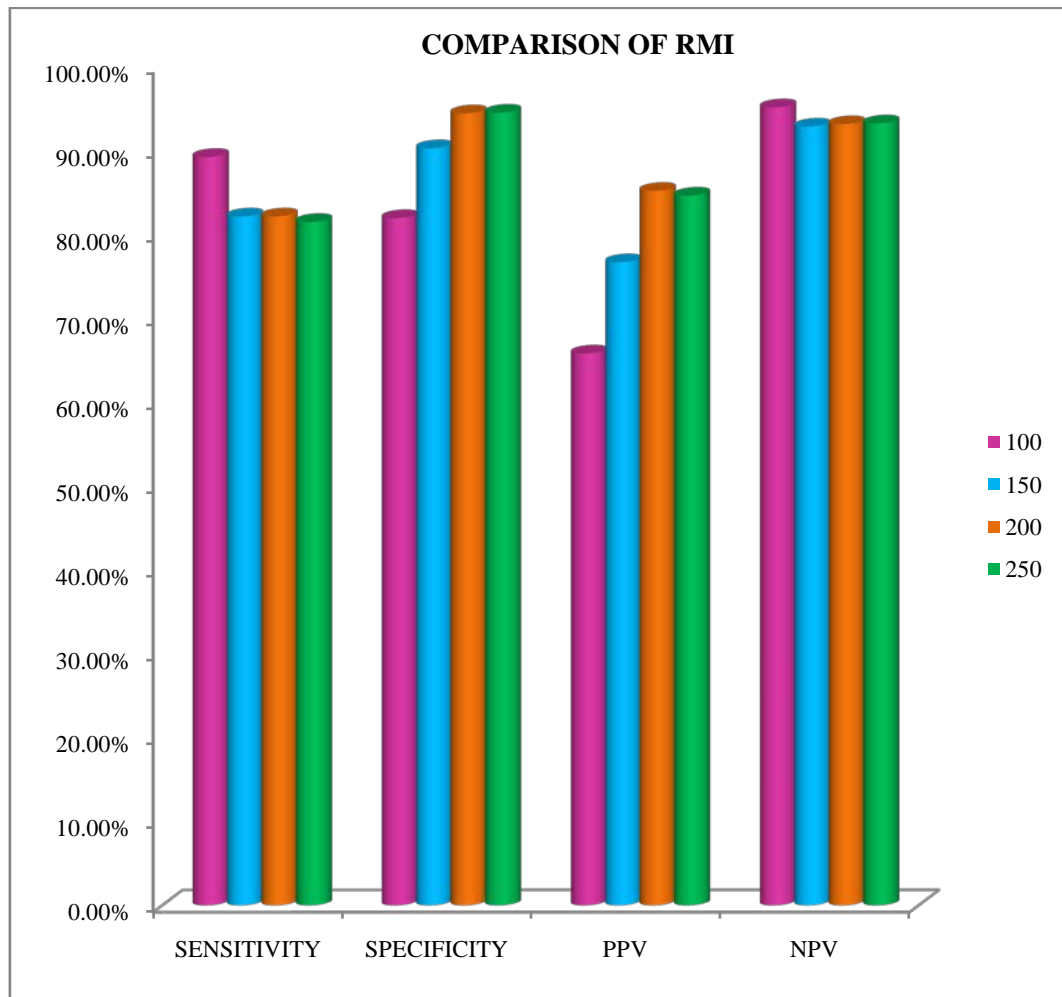




## COMPARISON OF RMI

<b>RMI</b>	<b>SENSITIVITY</b>	<b>SPECIFICITY</b>	<b>PPV</b>	<b>NPV</b>
100	89.24%	81.94%	65.79%	95.16%
150	82.14%	90.28%	76.67%	92.86%
200	82.14%	94.44%	85.19%	93.15%
250	81.48%	94.52%	84.62%	93.24%

The sensitivity of the RMI in discriminating benign and malignant ovarian tumor is high with the cut off value of 100. The sensitivity decreases as the cut off value of RMI is increased. The specificity of RMI is high with the cut off value of 250. Specificity increases with increase in the cut off value of RMI. Likewise the positive predictive value increases with increase in the cut off value of RMI. The positive predictive value is high at the cut off value of 250. The negative predictive value decreases with increase in the cut off value of RMI. The negative predictive value is high at the cut off value of 100. The optimal sensitivity, specificity, positive predictive value and negative predictive value for RMI is high at the cutoff value of 200. The cut off value of RMI at 200 is highly statistically significant, associated with the gold standard (HPE) i.e. malignant or benign.

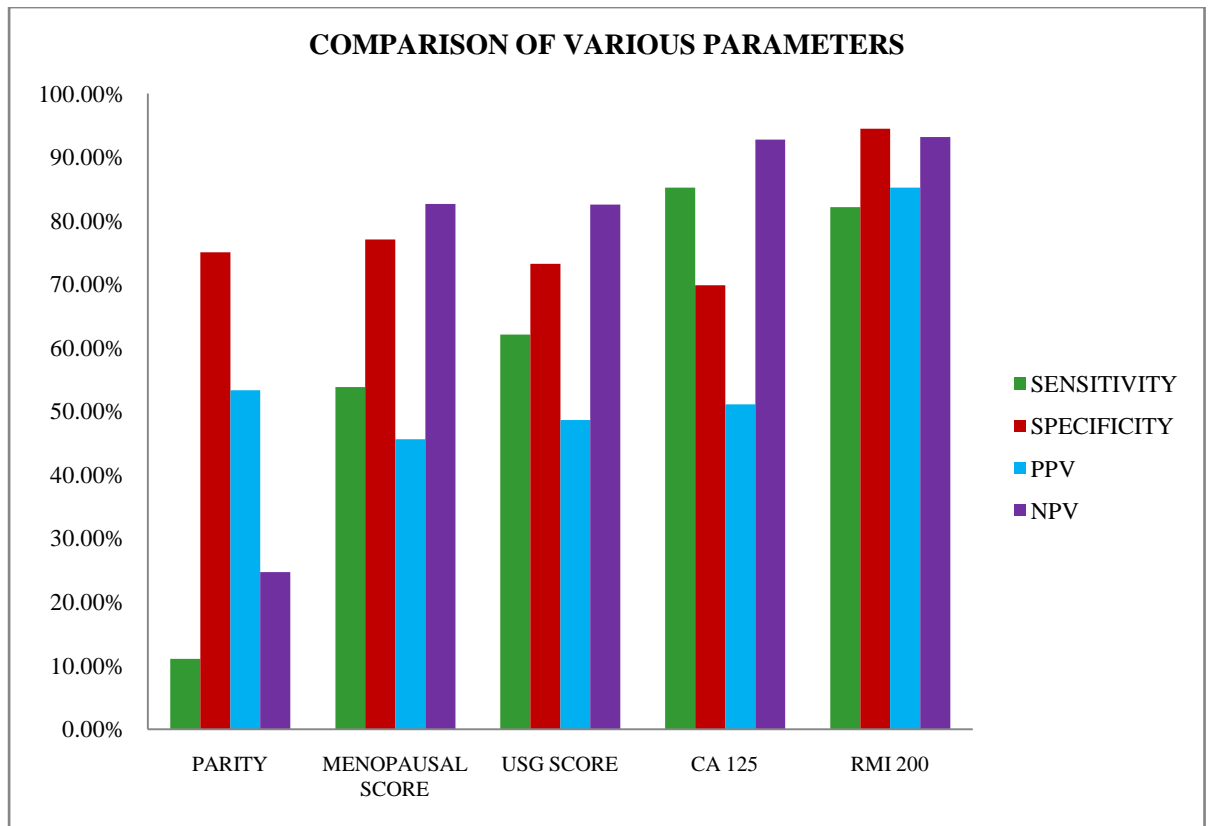


### COMPARISON OF VARIOUS PARAMETERS:

	<b>SENSITIVITY</b>	<b>SPECIFICITY</b>	<b>PPV</b>	<b>NPV</b>
PARITY	11.10%	75%	53.33%	24.71%
MENOPAUSAL SCORE	53.84%	77.02%	45.6%	82.61%
USG SCORE	62.07%	73.23%	48.64%	82.54%
CA 125	85.18%	69.86%	51.11%	92.73%
RMI	82.14%	94.44%	85.19%	93.24%

The sensitivity of parity as a diagnostic indicator is low %, 11.1% the specificity is high 75%, the positive predictive value is 53.33% and negative predictive value is 24.71% .

The diagnostic performance of sensitivity of menopausal score is 53.84%, specificity is 77.02%, positive predictive value is 45.61% and negative predictive value is 82.61%. Thus menopausal score has high Specificity and negative predictive value.



The sensitivity of ultrasound score as diagnostic modality in differentiating benign and malignant tumor is 62.06%, specificity is 73.23%, positive predictive value is 48.64% and negative predictive value is 82.54%. The specificity and negative predictive value are high for ultrasound score.

The sensitivity of CA 125 with a cut off value of 35 U/ml is 85.18%, specificity is 69.86%, positive predictive value is 51.11% and negative predictive value is 92.73%. CA 125 has high sensitivity and negative predictive value.

The diagnostic performance of sensitivity, specificity, positive predictive value and negative predictive value of RMI at cut off value of 200 are 82.14%, 94.42%, 85.19% and 93.15% respectively.

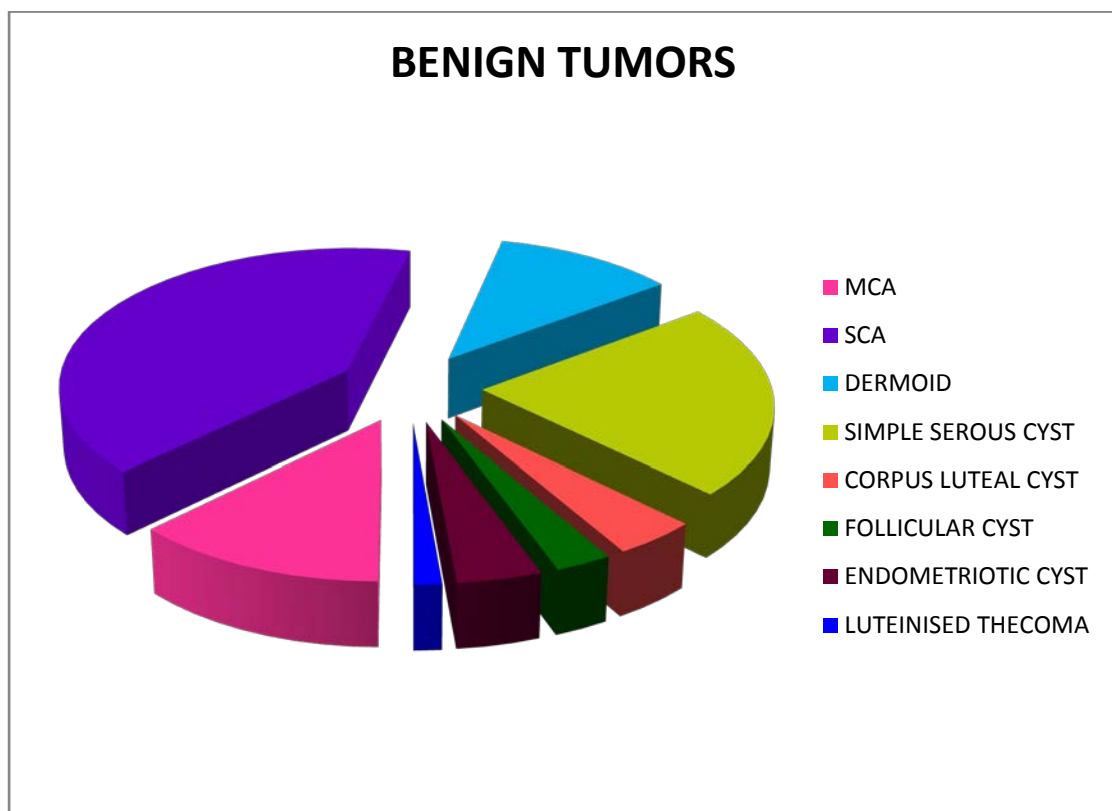
We found that RMI has better performance than CA 125, ultrasound score and menopausal score.

## BENIGN TUMORS

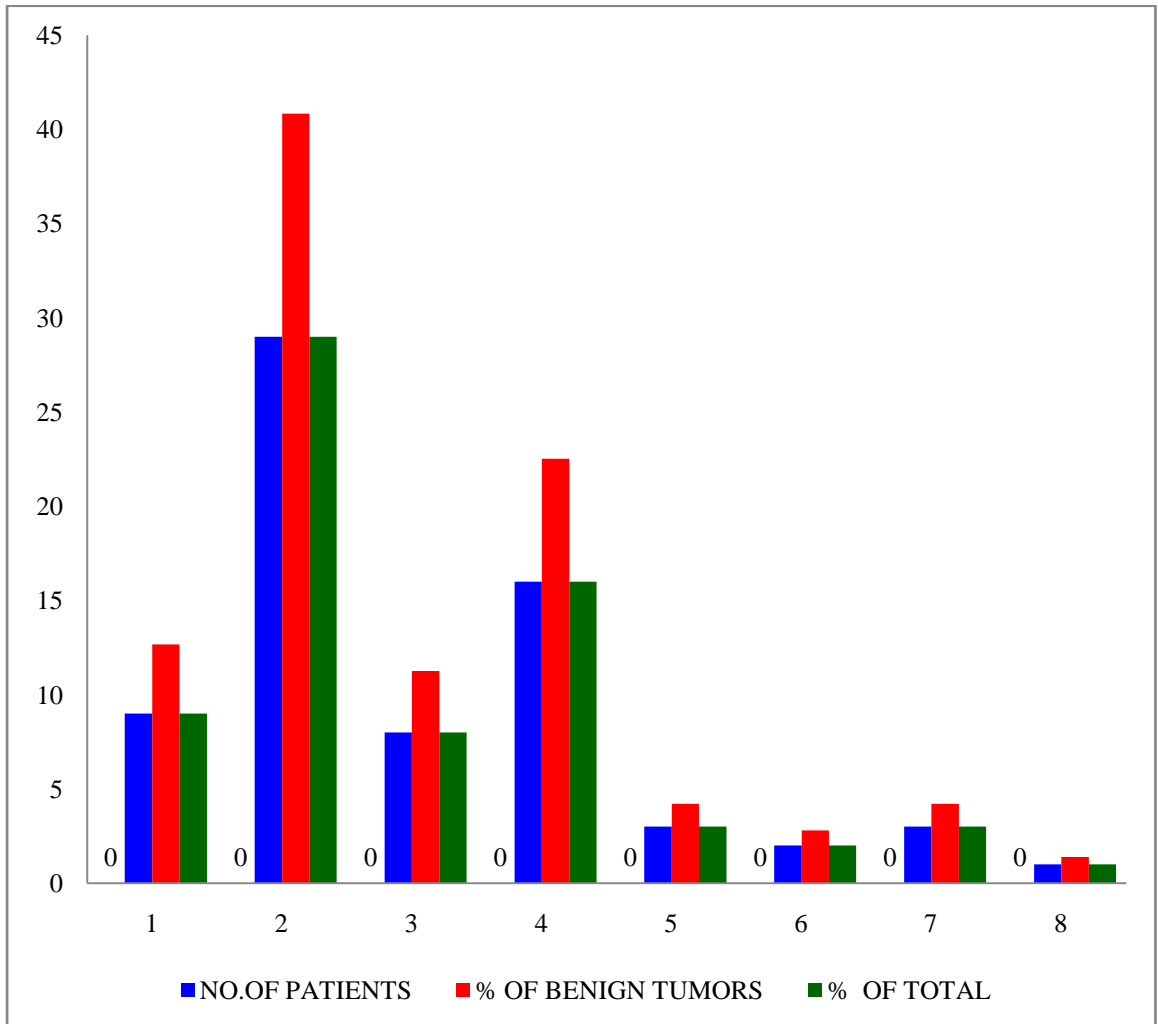
S.NO	HISTOPATHOLOGY	NO.OF PATIENTS	% OF BENIGN TUMORS	% OF TOTAL
1	MCA	09	12.67	9
2	SCA	29	40.84	29
3	DERMOID	08	11.26	8
4	SIMPLE SEROUS CYST	16	22.53	16
5	CORPUS LUTEAL CYST	03	4.22	3
6	FOLLICULAR CYST	02	2.81	2
7	ENDOMETRIOTIC CYST	03	4.22	3
8	LUTEINISED THECOMA	01	1.40	1

In this study serous cystadenoma is the most common tumor accounting 29% of the total tumor and 40.84% of the benign tumor. Simple serous cyst is the second most common which constitutes 16% of the total and 22.53% of the benign tumor. Next most common

tumor is the mucinous cystadenoma accounting for 9% of the total and 12.67% of the benign tumors.





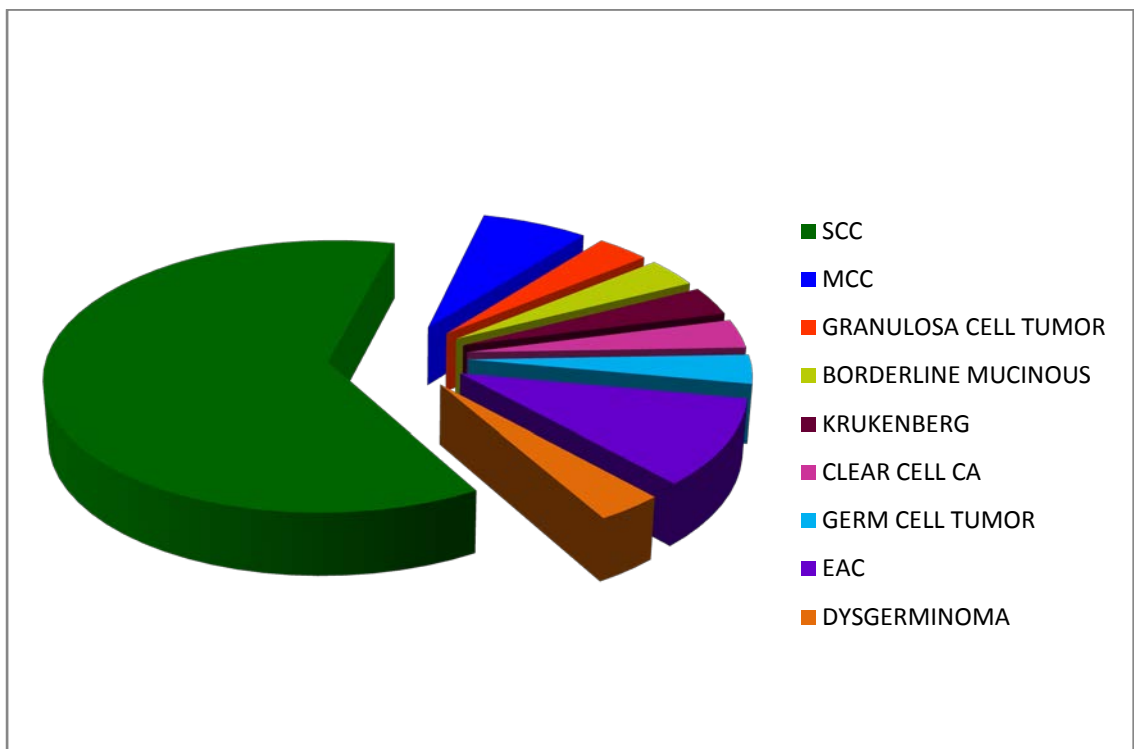


## MALIGNANT TUMORS

S.NO	HISTOPATHOLOGY	NO.OF PATIENTS	% OF MALIGNANT TUMORS	% OF TOTAL
1	SCC	18	62.06	18
2	MCC	02	6.89	2
3	GRANULOSA CELL TUMOR	01	3.44	1
4	BODERLINE MUCINOUS	01	3.44	1
5	KRUKENBERG	01	3.44	1
6	CLEAR CELL CA	01	3.44	1
7	GERM CELL TUMOR	01	3.44	1
8	ENDOMETRIOD ADENOCA	03	10.34	3
9	DYSGERMINOMA	01	3.44	1

In our study, the most common malignant tumor is papillary serous cystadenocarcinoma comprising 62.06% of patients with malignant cancer. It accounts for 18% of total patients. The second common

malignant tumor is mucinous cystadenocarcinoma accounting for 6.89% of malignant cases and 4.5% of total cases. The next tumors are endometrioid carcinoma accounting for 10.34% of malignant ovarian tumor.



## DISCUSSION

In our study, the peak incidence of the malignant ovarian tumor was 51-60 years of age during which 44.6% of ovarian tumors were malignant. The study shows that among those less than 40 years of age group, most of the neoplasms were benign and as age increases the risk of malignancy increases.

Various case control studies have shown that pregnancy reduces the risk of ovarian cancer. One pregnancy reduces the risk of ovarian cancer by as much as one third and with subsequent pregnancies the risk lowers further. Infertility has an increased risk of ovarian malignancy around 2 fold. In our study the ovarian mass among nulliparous women had more incidence of malignancy when compared to multiparous women. The study showed among nulliparous women 46.6% had malignant tumors compared to 24.7% in multiparous women.

On analysing the menstrual history, nearly half of the postmenopausal women had malignant ovarian tumor. Among menstruating women there was a slightly higher chance of malignancy in those with regular cycles when compared to patients with irregular cycle.

The study showed that the patients who had malignant ovarian neoplasm, most of them were in the postmenopausal status. 45.16% of

postmenopausal women had malignancy when compared to 17.39% in premenopausal women. Thus in postmenopausal women the malignant neoplasms are more common.

Sonographic evaluation of the structure of an ovarian mass in predicting the risk of malignancy have been reported. Many investigators have developed the objective Ultrasound score according to various ovarian morphologies to minimize the examiners descriptive interpretation which may be varied and not reproducible.

Many scoring systems based on various ultrasonographic morphologies have been made for this purpose. These scoring morphologies are tumor volume, number of localities, wall thickness, inner wall structure, septal structure, and shadowing or echogenicity or solid area . At different cut-off levels of Ultrasound scores as an indicator for discrimination of benign from malignant tumors, the sensitivity, specificity, positive predictive value (PPV) and a negative predictive value (NPV) from these studies ranged from 74- 88%, 40-65%, 28-36%, and 90-95%, respectively. Ferrazzi et al [45]., in1997, developed the new multicenter scoring system in determination of malignancy status of ovarian tumors based on the ultrasound morphology of the ovarian cyst wall, septae, vegetations,and echogenicity. The new scoring system yielded better result than the previous scoring systems reported in the

other studies with the accuracy, sensitivity, specificity, positive predictive value and negative predictive value of 72%, 87%, 67%, 41% and 95%, respectively.

For ultrasonographic technique in diagnosing ovarian cancer the sensitivity was 62% and specificity was 73% as shown in various study including Morgante et al<sup>(30)</sup> 1999, Leelahakorn et al<sup>(29)</sup> 2005.

In our study, the sensitivity of ultrasonographic score was 62.06% and specificity was 73.23%, the positive predictive value was 48.64% and negative predictive value was 82.94%.

The study showed that ultrasonogram of complex ovarian mass has more malignant potential. All though the value of CA 125 as a screening test for ovarian cancer is yet unsettled, its role for a differential diagnosis of ovarian mass is clearly established. CA125 a tumor marker for ovarian cancer is not specific. With a cut off value of 35 U/ml,

- True positive – 24 cases
- True negative – 40 cases
- False positive – 31 cases
- False negative – 5 cases

Among the five false negative cases, 2 cases were germ cell Tumor, one was granulosa cell tumor, one was krukemberg, and another one was serous cystadenocarcinoma.

Among 31 false positive cases, 24 cases were serous cystadenoma, 5 cases were mucinous cystadenoma.

CA 125 level has overall range of 6.7 - 832.64. The high values of CA 125 is found most commonly with papillary serous cystadenocarcinoma and endometrioid adenocarcinoma.

Benjapi bal et al [44], 2007 showed that CA 125 at the cut off level of 35 U/ml had the sensitivity of 83.1% and specificity of 39.3%. In 2010, Rachmasari putri et al study showed that CA 125 level at a cut off value of 35 U/ml had a sensitivity of 81.43% and specificity of 60%, positive predictive value of 87.69% and negative predictive value of 48%.

In our study, the sensitivity was 85.18% and the specificity was 69.85% the positive predictive value and the negative predictive value were 92.73% and 51.11% respectively. Our study showed that CA 125 has high sensitivity and high positive predictive value. The specificity was poor in predicting malignancy.

RMI was calculated using the formula for each patient included in the study (n=200). Out of 100 patients, the RMI with cut off value of 200, 68 patients had benign tumor and 24 patients had malignant tumor.

- True positive - 24 cases
- True negative -68 cases
- False positive -3 cases
- False negative - 5 cases

5 patients with RMI less than 200 had malignant ovarian cancer constituting false negative (6.8%). Out of 5 patients, 2 patients had germ cell tumor and 1 patients had mucinous cystadenocarcinoma, 1 had krukemberg and another one patient had granulosa cell tumor.

Among the 27 patients with RMI >200, 3 had benign tumors constituting the 14.81% of false positive cases. Out of 3 patients, 2 patients had serous cystadenoma and 1 patient had mucinous cystadenoma.

Thus serous cystadenoma was the most common cause of false positivity and germ cell tumor was the most common cause for false negativity.



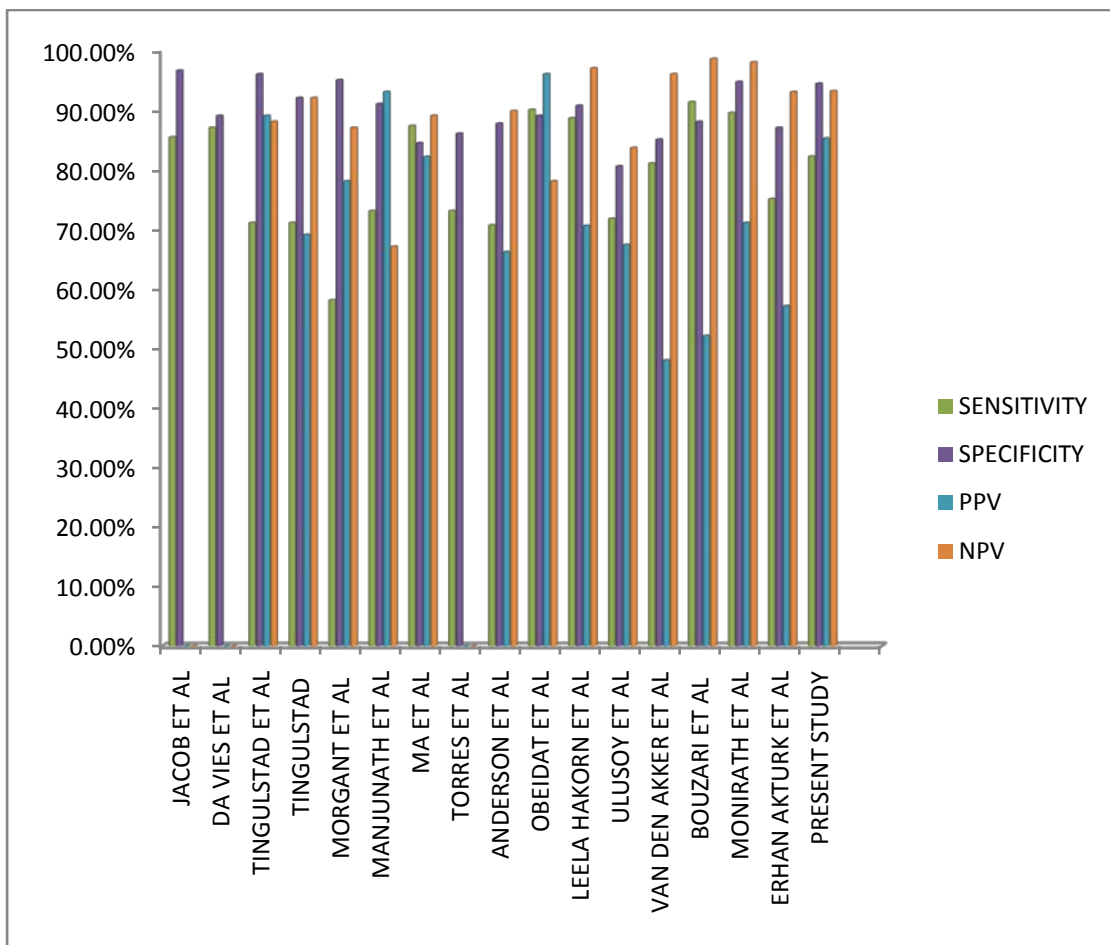
The false positive rates are important when a particular test has to be used in low risk populations diagnosed with ovarian mass during screening of ovarian abnormalities.

Among the benign tumors, the RMI had a range from 6.7 to 865.35. The mean RMI was 81.55 with SD 133.31. Among the malignant tumors the range is from 28.92 to 7493.76. The average RMI was 1158.44 with SD 1752.13. This was statistically significant.

In our study, the performance of sensitivity, specificity, positive predictive value and negative predictive value of RMI at various cutoff levels of 100, 150, 200, 250, were analysed. At a cut off level of 100, the RMI had highest sensitivity (89.24%) and negative predictive value (95.16%). The specificity (81.94%) and positive predictive value (65.79%) were low. As the cut off levels are increased, the sensitivity decreases and specificity increases. RMI at cut off value of 250, has the highest specificity (94.52%) and positive predictive value (84.62%). The sensitivity was low 81.48%. Multiple studies have shown that the best cut off value of RMI is 200. In our study, the performance of RMI at 200 is statistically significant as shown by the sensitivity 82.14%, specificity 94.4%, positive predictive value 85.19% and negative predictive value 93.15%.

## COMPARISON OF VARIOUS PREVIOUS STUDY WITH THE PRESENT STUDY

STUDY	YEAR	NO. OF PTS	SENSITI- VITY	SPECIFI- CITY	PPV	NPV
JACOB ET AL	1990	143	85.4%	96.6%	-	-
DAVIES ET AL	1993	124	87%	89%	-	-
TINGULSTAD ET AL	1996	173	71%	96%	89%	88%
TINGULSTAD	1999	365	71%	92%	69%	92%
MORGANTE ET AL	1999	124	58%	95%	78%	87%
MANJUNATH ET AL	2000	152	73%	91%	93%	67%
MA ET AL	2003	140	87.3%	84.4%	82.1%	89%
TORRES ET AL	2003	158	73%	86%	-	-
ANDERSON ET AL	2003	180	70.6%	87.7%	66.1%	89.8%
OBEIDAT ET AL	2004	100	90%	89%	96%	78%
LEELAHAKORN ET AL	2005	175	88.6%	90.7%	70.5%	97%
ULUSOY ET AL	2007	296	71.7%	80.5%	67.3%	83.6%
VAN DEN AKKER ET AL	2010	548	81%	85%	48%	96%
BOUZARI ET AL	2011	182	91.3%	88%	52%	98.58%
MONIRATH HAV ET AL	2011	151	89.5%	94.7%	71%	98%
ERHAN AKTURK ET AL	2012	100	75%	87%	57%	93%
PRESENT STUDY	2012	200	80%	96.8%	86.5%	92%



## SUMMARY

- 100 women with ovarian mass above 25 years of age were selected for the study. Patients with pregnancy are excluded.
- 44.8% patients were in the age group of 51- 60 years,31% in 41 – 50 years,13.7% in 30 - 40 years and 10.3% in >60 years.
- General and gynaecological examination was done for all cases.
- Ultrasound pelvis was done for all patients and the presence of bilateral ovarian mass, multiloculated tumor, presence of solid areas, ascites and extra ovarian metastasis were noted. An ultrasound score (U) of 1 was given if none or one of the features was found, and a score of 3 was given if two or more of these features were shown.
- Serum CA 125 level was measured preoperatively.
- Postmenopausal status was defined as more than one year of amenorrhea or age older than 50 years for women who had undergone hysterectomy; they were scored as M=3. All other patients who did not meet these criteria were defined in a premenopausal status which scored M=1.

- Risk of malignancy index was calculated based on RMI 3 (modified by Tingulstad [20] in 1999).
- Laparotomy was done for all cases and the specimen was sent for histopathological examination which is the gold standard.
- 79% of the tumor was benign and 21% was malignant.
- Prediction of malignancy by CA 125, ultrasound and RMI was compared and analysed.
- The optimal sensitivity, specificity, positive predictive value and negative predictive value for RMI were at the cut off value of 200.
- The diagnostic performance of sensitivity, specificity, positive predictive value and negative predictive value of RMI at cut off value of 200 were 82.14%, 94.44%, 85.19% and 93.15% respectively.
- Though CA 125 was highly sensitive (sensitivity was 85.18%), specificity and PPV were poor.
- The study showed that RMI has the better performance than CA 125, ultrasound score and menopausal score in the prediction of malignancy.

## **CONCLUSION**

Risk of malignancy index is a reliable method for differentiating benign and malignant ovarian mass preoperatively.

Risk of malignancy index is a multimodal approach that is simple and easily applicable in preoperative evaluation of patients with ovarian tumor.

Risk of malignancy index is a better diagnostic scoring index in discriminating benign and malignant tumor when compared to individual test of ultrasonogram or CA 125 level.

The optimal cut off point that best distinguishes benign from malignant ovarian mass for RMI is 200 in the present study.

RMI is the most useful diagnostic index in proper selection of patients who may require referral to tertiary care centers.

Since the specificity of Risk of malignancy index is high, there is a potential role for this index in selection of cases for conservative management or minimal invasive surgery of benign cases like ultrasound guided aspiration or laparoscopic excision of the cysts.

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## PROFORMA

NAME :                      AGE :                      IP NO :

SE CLASS :    RELIGION :

PRESENTING ILLNESS :      MASS

    DURATION

    PAIN ABDOMEN

    ABD DISTENSION

MENSTRUAL HISTORY :

MENOPAUSE :              YES              NO

MARRIED : YES              NO                      NO.OF YEARS:

OBSTETRIC HISTORY :                      NULLIPAROUS

PAROUS

NOC

LCB

OVULATION INDUCTION

CONTRACEPTION : YES                      NO

OCP

ST

OTHERS

PAST MEDICAL HISTORY : DM/HT/IHD/TB/

SURGICAL HISTORY : YES                      NO

**FAMILY HISTORY :**

OVARIAN MALIGNANCY

ENDOMETRIAL CA

BREAST CA.

**GENERAL EXAMINATION :**

HEIGHT:

WEIGHT:

BMI:

O/E :ANAEMIA

PEDAL EDEMA

LYMPH NODES

BREAST

THYROID

VITAL SIGNS: PR

BP

P/A :

MASS

ASCITES

OTHERS

P/S

P/V

USG ABDOMEN & PELVIS

<b>S.NO</b>	<b>USG FEATURES</b>	<b>PRESENT</b>	<b>ABSENT</b>
1	MULTISEPTATIONS		
2	SOLID COMPONENTS		
3	BILATERALITY		
4	ASCITES		
5	METASTASIS		

ULTRASOUND SCORE :

CA 125 VALUE :

MENOPAUSAL SCORE :

RISK OF MALIGNANCY INDEX :

LAPAROTOMY FINDINGS

HPE



## **CONSENT FORM**

### **STUDY TITLE :**

STUDY OF RISK OF MALIGNANCY INDEX WITH  
HISTOPATHOLOGICAL EXAMINATION IN OVARIAN TUMORS.

### **STUDY CENTRE :**

Department of Obstetrics and Gynaecology, Tirunelveli Medical  
College And Hospital, Tirunelveli.

Participant Name:      Age:      Sex:      I.D.No.:

I confirm that I have understood the purpose of the above study. I  
have the opportunity to ask the questions and all my questions and doubts  
have been answered to my satisfaction.

I understand that my participation in the study is voluntary and that  
I am free to withdraw at any time without giving any reason.

I understand that the investigator, regulatory authorities and the  
ethics committee will not need my permission to look at my health  
records both in respect to the current study and any further research that  
may be conducted in relation to it, even if I withdraw from the study. I  
understand that my identity will not be revealed in any information  
released to third parties or published, unless as required under the law.

I agree not to restrict the use of any results that arise from the study. I hereby consent to participate in this study titled “STUDY OF RISK OF MALIGNANCY INDEX WITH HISTOPATHOLOGICAL EXAMINATION IN OVARIAN TUMORS”

Signature of Investigator:

Study Investigators Name:

Signature/thumb impression of patient

Date :

Thanking you,

Place :

## BENIGN

- MUCINOUS CYSTADENOMA(MCA)-9
- SEROUS CYSTADENOMA(SCA)-29
- DERMOID-8
- SIMPLE SEROUS CYST-16
- CORPUS LUTEAL CYST-3
- FOLLICULAR CYST-2
- ENDOMETRIOTIC CYST-3
- LUTEINISED THECOMA-1
- TOTAL-71

## MALIGNANT

- SEROUS CYSTADENOMA CARCINOMA(SCC)-18
- MUCINOUS CYSTADENOCARCINOMA(MCC)-2
- GRANULOSA CELL TUMOR-1
- BORDERLINE MUCINOUS-1
- KRUKENBERG-1
- CLEAR CELL CA-1
- GERM CELL TUMOR-1
- ENDOMETRIOID ADENOCA-3
- DYSGERMINOMA-1
- TOTAL-29

## KEY TO THE MASTER CHART

RMI	-	Risk of Malignancy Index
USG	-	Ultrasonogram
NG	-	NulliGravida
REG	-	Regular
IRREG	-	Irregular
PMB	-	Post Menopausal Bleeding
ABD	-	Abdomen
MNP	-	Menopause
P	-	Para
L	-	Live
A	-	Abortion
ST	-	Sterlised
HPE	-	Histopathological Examination
SCA	-	Serous Cystadenoma
MCA	-	Mucinous Cystadenoma
PSCC	-	Papillary Serous Cystadeno Carcinoma
MCC	-	Mucinous Cystadeno Carcinoma
SCC	-	Serous Cystadeno Carcinoma
GCT	-	Granulosa Cell Tumor
EAC	-	Endometroid Adeno Carcinoma
MNP	-	Menopausal

S. NO	Sl.No	NAME	AGE	IP NO	COMPLAINTS	MENSTRUAL	PARITY	MENOPAUSAL SCORE	USG	CA 125	RMI SCORE	HPE
						HISTORY			SCORE			
1	1	MARIYAPUSHPAM	55	23882	ABD.DISTENSION	MNP-8	P4L4/ST	3	1	19	57	MCA
2	2	LINGAMMAL	55	55314	ABD PAIN	MNP-7	P4L3/ST	3	3	312.6	2813.4	SCC
3	3	SELVI	50	23451	ABD.DISTENSION	MNP-4	P4L3	3	1	42	126	KRUKENBERG
4	4	PUTHIYAL	55	54674	ABD.DISTENSION	MNP-6	P3L2	3	1	10.5	31.5	SIMPLE SEROUS CYST
5	5	MUTHAMMAL	50	17800	ABD.DISTENSION	MNP-4	P4L3	3	1	9.8	29.4	SCA
6	6	DRAVIDASELVI	48	15099	PAIN	RG	P3L3	1	1	6.9	6.9	SIMPLE SEROUS CYST
7	7	MUTHUMARI	30	17112	ABD.DISTENSION		P2L2	1	1	6.7	6.7	MCA
8	8	DEIVANAI	65	28909	ABD PAIN , ABD.DISTENSION	MNP-12	P7L7	3	1	750	2250	SCC
9	9	SELVARANI	39	26366	ABD PAIN	RG	P2L2/ST	1	1	18.6	18.6	SCA
10	10	DHANALAKSHMI	49	22535	ABD PAIN	IRRG	P3L3	1	3	198.4	595.2	SCC
11	11	PUSHPAM	55	22181	ABD PAIN	MNP-7	P1L0	3	3	878.3	7904.7	SCC
12	12	DEIVANAI	57	14411		MNP-5	P5L5	3	3	75.6	680.4	MUCINOUS BORDERLE TUMOR
13	13	MUTHURAMAYEE	48	55698	ABD PAIN	MNP-2	P3L2	3	3	8.5	76.5	SIMPLE SREOUS CYST
14	14	KASTHURI	55	53940	ABD PAIN, ABD.DISTENSION	MNP-4	NP	3	3	600	5400	SCC
15	15	MUTHUSELVI	26	34256	ABD PAIN	RG	P2L2	1	1	27	27	CORPUS LUTEAL CYST
16	16	VIJAYALAKSHMI	32	16170	ABD.DISTENSION	IRRG	P2L2	1	1	9	9	MCA
17	17	MADATHY	65	15068	ABD.DISTENSION	RG	P4L4	3	3	600	5400	SCC
18	18	VASANTHA	40	18890	ABD.DISTENSION	RG	P2L2	1	3	184.2	552.6	CLEAR CELL CA
19	19	VIJAYALAKSHMI	32	16170	ABD.DISTENSION	RG	P2L2	1	1	9	9	SIMPLE SEROUS CYST
20	20	SHANMUGAM	42	13468	ABD PAIN	MNP-2	P3L3	1	1	123	123	SCA
21	21	BALASUBBULAKSHMI	21	6677	ABD.DISTENSION	RG	NP	1	1	17	17	SCA
22	22	ESAKKIAMMAL	30	51418	ABD PAIN , ABD.DISTENSION	RG	NP	1	1	956.2	956.2	ENDOMETRIOID ADENOCA
23	23	KUTTITHAI	55	49856	ABD PAIN	MNP-6	P4L4	3	3	177.5	1597.5	SCC
24	24	RAJAMUNISHA	20	10732	ABD PAIN	RG	NP	1	1	14.1	14.1	FOLLICULAR CYST
25	25	CHELLAMMAL	58	28164	ABD PAIN	MNP-9	P7L6	3	1	415.5	1246.5	MCC
26	26	MAHALAKSHMI	58	40803	ABD.DISTENSION	MNP-9	P4L3	3	3	32	288	MCA
27	27	MALAYAMMAL	49	45632	ABD.DISTENSION	MNP-2	P3L2	3	1	3000	9000	SCC
28	28	RAJAMMAL	41	13456	ABD PAIN	RG	P2L2	1	1	946	946	SCC
29	29	KASTHURI	55	53940	ABD PAIN , ABD.DISTENSION	MNP-6	NP	3	1	6000	18000	SCC
30	30	SUBBAMMAL	68	56701	ABD PAIN	MNP-16	P10L6	3	1	29	87	SCA
31	31	APARNA	14	13643	ABD.DISTENSION	IRRG	NP	1	1	9.9	9.9	SIMPLE SEROUS CYST

32	32	JEYAVALLI	30	45103	ABD PAIN	RG	P3L3	1	1	13	13	DERMOID
33	33	ESAKKIAMMAL	36	70798	ABD PAIN	RG	NP	1	3	48	144	SCA
34	34	VAIRAMUTHU	45	51216	ABD PAIN	RG	P2L2	1	3	10.6	31.8	DERMOID
35	35	LAKSHMI	41	52929	ABD PAIN	IRRG	P3L3	1	3	19.42	19.42	MCA
36	36	PUNITHAMALAR	34	10884	ABD PAIN	RG	P3L3/ST	1	1	15.8	15.8	SIMPLE SEROUS CYST
37	37	SUBBALAKSHMI	36	8750	ABD PAIN	RG	P2L2/ST	1	1	13	13	SIMPLE SEROUS CYST
38	38	LATHA	45	3124	ABD DISTENTION	IRRG	P3L3/ST	1	3	198.74	596.22	SCC
39	39	SAKUNTHALA	45	5673	ABD.DISTENSION	RG	P3L3/ST	1	3	64.1	192.3	SCA
40	40	RAMALAKSHMI	54	14193	PAIN , ABD.DISTENSION	MNP-6	P3L3/ST	3	3	60.1	540.9	SCA
41	41	THANGAM	52	15756	ABD.DISTENSION	MNP-4	P3L3	3	3	19.42	174.78	MCA
42	42	CHANDRA	45	19529	ABD.DISTENSION	REG	P2L2/ST	1	3	9.35	28.05	DERMOID
43	43	KANNIAMMAL	32	23911	ABD PAIN	REG	P2L1A2	1	1	64.16	64.16	SCA
44	44	MAHALAKSHMI	35	27577	ABD PAIN	IRREG	P2L2/ST	1	1	69.49	69.49	SCA
45	45	PAKKIYATHAI	40	25804	ABD PAIN	REG	P2L2	1	1	10.67	10.67	SIMPLE SEROUS CYST
46	46	LAKSHMI	50	28683	ABD.DISTENSION	MNP-4	P4L2/ST	3	3	56.92	512.28	SCC
47	47	MUTHAMMAL	55	27570	PAIN	MNP-2	P2L2/ST	3	1	10.9	32.7	GRANULOSA CELL TUMOR
48	48	THAMBIRATTI	53	27091	ABD.DISTENTION	MNP-4	P4L2/ST	3	3	56.92	512.28	SCC
49	49	KALAIMATHI	51	30565	ABD PAIN	REG	P2L2	1	1	10.67	10.67	SIMPLE SEROUS CYST
50	50	PANEER	40	30297	ABD PAIN	RG	P1L1	1	3	26.9	80.7	DERMOID
51	51	VIJAYA	34	55261	ABD PAIN	RG	P1L2	1	1	11.5	11.5	DERMOID
52	52	PETCHIAMMAL	49	58221	ABD DISTENSION	IRRG	P4L2/ST	1	3	727.18	2181.54	EAC
53	53	BANUPRIYA	15	45632	ABD PAIN	RG	P3L3/ST	1	1	16.86	16.86	SIMPLE SEROUS CYST
54	54	MUTHULAKSHMI	25	53078	ABD PAIN	RG	P2L2	1	1	6.7	6.7	SIMPLE SEROUS CYST
55	55	MUPPIDATHY	30	54653	ABD PAIN	RG	P2L2/ST	1	1	9.03	9.03	DERMOID
56	56	MUPPIDATHY	32	56585	ABD PAIN	IRRG	NP	1	1	7.12	7.12	ENDOMETRIOTIC CYST
57	57	SUDHA	36	59466	ABD PAIN	RG	P3L3/ST	1	3	59.37	178.11	SCA
58	58	MARY	23	22319	ABD PAIN	RG	P2L2	1	1	7.3	7.3	SIMPLE SEROUS CYST
59	59	MUPPIDATHY	32	57131	ABD DISTENSION	RG	P2L2	1	3	8.2	24.6	DYSGERMINOMA
60	60	MARIAMMAL	45	57656	ABD PAIN	RG	P2L2	1	3	49.35	148.05	SCA
61	61	BOMMUAMMAL	65	60220	ABD PAIN	RG	P3L3	1	3	81.8	245.4	SCA
62	62	MARIAMMAL	39	59146	ABD PAIN	RG	P3L2	1	1	87.19	87.19	SCA
63	63	MARIAMMAL	38	58968	ABD PAIN	IRRG	P2L2	1	1	5.6	5.6	CORPUS LUTEAL CYST
64	64	SUSILA	42	63388	ABD DISTENTION	RG	P4L2/ST	1	3	731.84	2195.5	ENDOMETRIOID ADENO CA
65	65	MARIAMMAL	52	66537	ABD DISTENTION	MNP-6	NP	3	1	101.41	304.23	SCC

66	66	LAKSHMI	61	66211	ABD PAIN	MNP-1	P2L2/ST	3	1	9.64	28.92	GERM CELL TUMOR
67	67	SAMIDAYAL	62	68344	ABD DISTENTION	MNP-8	P6L3	3	3	52.6	473.4	MCA
68	68	CHINNAMMAL	24	73152	ABD PAIN	IRREG	P2L2	1	3	43.65	130.95	SCA
69	69	PAULTHAI	35	72967	ABD PAIN	RG	P2L2/ST	1	1	8.35	8.35	SIMPLE SEROUS CYST
70	70	SELVI	40	70181	ABD PAIN	RG	P3L3/ST	1	1	16.86	16.86	SIMPLE SEROUS CYST
71	71	SUBBULAKSHMI	33	13076	ABD PAIN	IRRG	P2L2/ST	1	1	71.48	71.48	SCA
72	72	SUMATHY	30	5764	ABD PAIN	IRRG	P2L2/ST	1	1	10.41	10.41	CORPUS LUTEAL CYST
73	73	THAVAMANI	47	4469	ABD PAIN	RG	P5L2	1	3	20.74	62.22	SCA
74	74	MAHARASI	50	6400	ABD PAIN	MNP-2	P4L3/ST	3	1	24.65	73.95	SCA
75	75	KALYANI	45	7968	ABD PAIN	RG	P3L2/ST	1	1	19.82	19.82	SCA
76	76	PACKIYATHAI	35	6843	ABD PAIN	IRRG	P1L1	1	1	7.8	7.8	ENDOMETRIOTIC CYST
77	77	LAKSHMI	57	9339	ABD DISTENTION	MNP-14	P6L4/ST	3	3	420.64	3785.76	SCC
78	78	PARVATHY	46	35132	ABD PAIN	RG	P2L2	1	1	10.6	10.6	SIMPLE SEROUS CYST
79	79	MUTHAMMAL	38	36986	ABD PAIN	IRRG	P1L1	1	1	13.2	13.2	ENDOMETRIOTIC CYST
80	80	SARATHA	55	35822	ABD PAIN	RG	P1L2	1	1	11.53	11.53	DERMOID
81	81	SHANTHI	46	35549	ABD PAIN	IRRG	P2L2	1	3	44.82	134.46	SCA
82	82	LOGANAYAKI	51	21324	ABD.DISTENSION	MNP-2	NP	3	3	498.4	4485.6	SCC
83	83	VALLI	41	36324	ABD PAIN	RG	NP	1	3	380.1	1140.3	SCC
84	84	CHANDRA	32	36424	ABD PAIN	RG	P1L0	1	1	55.39	55.39	SCA
85	85	MAHESHWARI	36	27364	ABD.DISTENSION	RG	P2L2/ST	1	3	12.48	37.44	SCA
86	86	ANJALI	45	26424	ABD.DISTENSION	IRRG	P3L3	1	3	14.6	43.8	MCA
87	87	MUTHUDEVI	31	21362	ABD.DISTENSION	IRRG	P2L2/ST	1	1	14.74	14.74	MCA
88	88	LAKSHMI	34	22632	ABD PAIN	RG	P2L2/ST	1	1	62.58	62.58	SCA
89	89	CHINNAPONNU	46	23134	ABD PAIN	IRRG	P2L2/ST	1	1	72.48	72.48	SCA
90	90	SUMATHY	30	34526	ABD PAIN	RG	P1L1	1	1	27.4	27.4	SCA
91	91	SUNDARI	46	23469	ABD PAIN	RG	P5L2	1	1	18.3	18.3	LUTEINISED THECOMA
92	92	KARPAGAVALLI	33	53024	ABD PAIN	IRRG	P2L2/ST	1	1	10	10	FOLLICULAR CYST
93	93	BACKIYALAKSHMI	56	19645	ABD.DISTENSION	MNP-12	NP	3	1	10.5	31.5	SCC
94	94	SAVITHRI	34	3624	ABD PAIN	RG	P2L2/ST	1	1	72.8	72.8	SCA
95	95	VANITHA	40	67435	ABD PAIN	RG	P3L2	1	1	87.1	87.1	SCA
96	96	PARVATHY	55	10364	ABD PAIN, ABD.DISTENSION	MNP-3	NP	3	3	12	108	MCC
97	97	PITCHAMMAL	50	10462	ABD PAIN	IRRG	P5L5/ST	1	1	75	75	SCA
98	98	RANI	32	14220	ABD PAIN	RG	P2L2/ST	1	1	8.3	8.3	SIMPLE SEROUS CYST
99	99	KALAIVANI	55	17321	ABD.DISTENSION	MNP-6	P3L3	3	1	46.28	138.84	SCA
100	100	KUMARI	30	17643	ABD PAIN	RG	NP	1	1	9.4	9.4	DERMOID